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RECENT ADVANCES IN THE TREATMENT OF VIRAL AND RICKETTSIAL DISEASES

THOMAS M. RIVERS, M.D.
New York

Brilliant results obtained in the therapy of certain bacterial and spirochetal diseases by the use of chemical agents and antibiotics emphasize the absence of similar successes in the treatment of viral and rickettsial diseases. This difference between the response of bacterial and spirochetal diseases on the one hand and viral and rickettsial diseases on the other to chemotherapy is probably due to fundamental differences in the nature and metabolic activities of the two groups of disease-producing agents.

Although nothing similar to the therapeutic results obtained with bacterial and spirochetal diseases can be pointed to in the viral and rickettsial field, sufficient evidence has been obtained to warrant the hope that eventually chemotherapeutic agents and antibiotics will be found effective against maladies in the latter group. For instance, Meiklejohn and his associates [1] and Wiseman and his associates [2] have reported that penicillin and sulfadiazine have some therapeutic value when used against certain strains of viruses in the psittacosis-lymphogranuloma group. Greiff and Pinkerton [3] have shown that experimental rickettsial infections are somewhat susceptible to the action of penicillin, while other workers [4] have found them to be susceptible to para-aminobenzoic acid and nitroacridine. It has also been shown that nitroacridine has an inhibitory effect on the growth of influenza B virus in embryonated eggs.[5] Fitzgerald and Lee [6] found that "phosphine GRN" (2-amino-9 [*p*-aminophenyl] acridinium chloride) effectively inhibits the multiplication of a bacteriophage in infected suspensions of Escherichia coli. This inhibition is counteracted by ribonucleic acid, a result which suggests that some cellular mechanism involving nucleic acid or related substances is essential for the multiplication of the bacteriophage. According to Cohen and Anderson,[7] 5-methyl tryptophane inhibits multiplication of E. coli B without apparent effect on the rate of its oxygen utilization in a synthetic medium. E. coli organisms infected with bacteriophage T2 or T4 do not support the reproduction of the viruses while in the presence of 5-methyl tryptophane, a substance which has no deleterious effect on the bacteriophages exposed to it in the absence of bacteria. While bacteriophages do not multiply in bacteria in the presence of 5-methyl tryptophane, they are able to do so when it is removed from the bacteria by dilution. Horsfall and McCarty [8] have shown that several polysaccharides, such as those obtained from Klebsiella pneumoniae and Streptococcus MG, have a therapeutic action in mice suffering from pneumonia caused by a virus designated as PVM (pneumonia virus of mice). This pneumonia can be produced only by intranasal introduction of the virus, and the polysaccharide, if a therapeutic effect is desired, also must be introduced intranasally. The maximum multiplication of the virus in the lungs is reached on the sixth or seventh day, at which time most mice die. Polysaccharides introduced as late as the fourth day after infection will protect the animals from death. While the virus is not inactivated by the polysaccharides, it is unable to multiply in their presence. Takahashi [9] has reported that a polysaccharide from yeast inactivates tobacco mosaic virus and believes that the inactivation is brought about through a reaction between the polysaccharide and some group in the virus particle which is essential for its infectivity. Other workers, however, are of the opinion that the yeast polysaccharide produces the observed results by action on the host cells instead of on the virus. Snyder [10] has emphasized the fact that para-aminobenzoic acid used in experimental rickettsial infections in embryonated eggs does not destroy or kill the

From the Hospital of the Rockefeller Institute for Medical Research.

Read in a Panel Discussion on Recent Advances in Treatment before the joint meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 13, 1947.

1. Meiklejohn, G.; Wagner, J. C., and Beveridge, G. W.: Studies on the Chemotherapy of Viruses in the Psittacosis-Lymphogranuloma Group: I. Effect of Penicillin and Sulfadiazine on Ten Strains in Chick Embryos, J. Immunol. **54:** 1-8 (Sept.) 1946.

2. Wiseman, R. W.; Meiklejohn, G.; Lackman, D. B.; Wagner, J. C., and Beveridge, G. W.: Studies on the Chemotherapy of Viruses in the Psittacosis-Lymphogranuloma Group: II. Effect of Penicillin and Sulfadiazine on Seven Strains in Mice, J. Immunol. **54:** 9-16 (Sept.) 1946.

3. Greiff, D., and Pinkerton, H.: Inhibition of Growth of Typhus Rickettsiae in the Yolk Sac by Penicillin, Proc. Soc. Exper. & Med. **55:** 116-119 (Feb.) 1944.

4. Snyder, J. C.; Maier, J., and Anderson, C. R.: Report to the Division of Medical Sciences, National Research Council, Washington, D. C., Dec. 26, 1942. Greiff, D.; Pinkerton, H., and Moragues, V.: Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae: I. Penicillin, Para-Aminobenzoic Acid, Sodium Fluoride, and Vitamins of the B Group, J. Exper. Med. **80:** 561-574 (Dec.) 1944. Hamilton, H. L.; Plotz, H., and Smadel, J. E.: Effect of *p*-Aminobenzoic Acid on the Growth of Typhus Rickettsiae in the Yolk Sac of the Infected Chick Embryo, Proc. Soc. Exper. Biol. & Med. **58:** 255-262 (March) 1945. Hamilton, H. L.: Effect of *p*-Aminobenzoic Acid on Growth of Rickettsiae and Elementary Bodies, with Observations on Mode of Action, ibid. **59:** 220-226 (June) 1945.

5. Green, R. H.; Rasmussen, A. F., Jr., and Smadel, J. E.: Chemoprophylaxis of Experimental Influenza Infections in Eggs, Pub. Health Rep. **61:** 1401-1403 (Sept. 27) 1946.

6. Fitzgerald, R. J., and Lee, M. E.: Studies on Bacterial Viruses: II. Observations on the Mode of Action of Acridines in Inhibiting Lysis of Virus-Infected Bacteria, J. Immunol. **52:** 127-135 (Feb.) 1946.

7. Cohen, S. S., and Anderson, T. F.: Chemical Studies on Host-Virus Interactions: I. The Effect of Bacteriophage Adsorption on the Multiplication of Its Host, Escherichia Coli B, with an Appendix Giving Some Data on the Composition of the Bacteriophage, T2, J. Exper. Med. **84:** 511-526 (Nov.) 1946; II. Chemical Simulation of the Interference Phenomenon by 5-Methyl Tryptophane, ibid. **84:** 525-533 (Nov.) 1946.

8. Horsfall, F. L., Jr., and McCarty, M.: The Modifying Effects of Certain Substances of Bacterial Origin on the Course of Infection with Pneumonia Virus of Mice (PVM), J. Exper. Med. **85:** 623-646 (June) 1947.

9. Takahashi, W. N.: Properties of a Virus Inactivator from Yeast, Science **104:** 377 (Oct. 18) 1946.

10. Snyder, J. C.: Personal communication to the author.

rickettsias already present; it merely inhibits further multiplication of them.

Sufficient examples have been cited to show that progress has been made in the treatment of experimental viral and rickettsial diseases by means of chemical agents and antibiotics. There is also evidence that penicillin and sulfonamide compounds are efficacious in the treatment of human diseases caused by viruses in the psittacosis-lymphogranuloma group and that para-aminobenzoic acid given in sufficient amounts and often enough has value in the treatment of human diseases caused by rickettsias, namely, epidemic typhus, murine typhus, scrub typhus and Rocky Mountain spotted fever.[11] However, according to Snyder,[10] para-aminobenzoic acid is of value only when it is given early in the course of illness, because within a week sufficient damage to the vascular system of the human body has usually been accomplished by rickettsias to cause death of a patient even though no further multiplication of them takes place.

At this point it should be emphasized that, with the exception of diseases in the psittacosis-lymphogranuloma and the typhus–Rocky Mountain spotted fever groups, viral and rickettsial maladies of human beings do not respond to known chemotherapeutic agents and antibiotics. Therefore, indiscriminate use of these substances in the treatment of such diseases of man is inexcusable. In view of what has been accomplished, there is reason to believe that potent therapeutic agents for many of these diseases will be discovered. In the meantime, however, practicing physicians should be aware of the limitations of this kind of therapy with the agents already at hand. Diagnosis and treatment of infectious diseases should be based on clinical skill and laboratory precision instead of chemotherapeutic and antibiotic trial and error.

A striking feature about the results of work on chemotherapy of experimental viral and rickettsial diseases is that the viruses and rickettsias themselves are not inactivated or injured by the substances used; all that happens is that further multiplication of the disease-producing agents ceases. This is quite different from what takes place when bacteria and spirochetes come in contact with chemotherapeutic agents and antibiotics. In most instances, these micro-organisms are killed by adequate concentrations of the therapeutic substances, and their death is believed to be brought about by an interference with certain of their enzyme systems or metabolic processes. Most bacteria and spirochetes, possessing all the enzyme systems essential for growth and reproduction, are not dependent on host cells. On the other hand, viruses and rickettsias are intracellular parasites and are believed not to possess complete enzyme systems essential for multiplication. If this is true, then such systems are supplied wholly or in part by their host cells. Furthermore, if viruses and rickettsias do not have enzyme systems of their own, then therapeutic agents can have no direct, deleterious effect on them through disruption of such systems; nevertheless, their activities and multiplication can be interfered with indirectly through the action of therapeutic agents which disturb certain enzyme systems and metabolic processes of their host cells. What has just been said offers a logical explanation of why known chemotherapeutic agents and antibiotics yield different results in different kinds of infectious diseases and indicates a practicable approach to therapeutic problems in the viral and rickettsial field.

11. (*a*) Ravenel, S. F.: Para-Aminobenzoic Acid Therapy of Rocky Mountain Spotted Fever, J. A. M. A. **133**: 989-994 (April 15) 1947. (*b*) Smith, P. K.: The Use of Para-Aminobenzoic Acid in Endemic (Murine) Typhus, ibid. **131**: 1114-1117 (Aug. 3) 1946.

ABSTRACT OF DISCUSSION

HEPATITIS FOLLOWING TRANSFUSIONS

QUESTION: Is there any method of preventing hepatitis following transfusions from blood or plasma?

ANSWER: As yet there is no definite means of preventing this kind of hepatitis. Dr. Joseph Stokes Jr. and his associates are conducting experiments with human globulin given at least twice at monthly intervals after the administration of blood or plasma. The evidence that globulin given in this manner is efficacious is not as yet conclusive.

NO PREVENTIVE OF THE COMMON COLD

QUESTION: Is there any hope of developing methods to prevent the common cold?

ANSWER: There are no methods at present of preventing the common cold. Of course, persons working in the field of medical research hope some day to find a means of preventing this disease.

POLIOMYELITIS

QUESTION: What can be done to prevent poliomyelitis?

ANSWER: At present no method is known by which this disease can be prevented. Vaccines are not available for use in human beings. There is doubt whether prophylaxis by means of convalescent serum is practicable. The virus is widespread during epidemic periods, being found in great quantities in the feces of patients with paralysis, patients with abortive poliomyelitis, persons with inapparent infection with poliomyelitis and many contacts. The virus is also found at times in the secretions of the upper respiratory tract. Many workers believe that the disease is spread by contact, the virus getting from feces and secretions of the upper respiratory tract of patients, etc., to the mouths of susceptible persons. If what has been said is true, it will be difficult to put into effect measures of control.

TREATMENT OF VIRAL DISEASES

QUESTION (Dr. J. Greengard, Chicago): Do human convalescent serums have an important place in the therapy of viral diseases?

ANSWER: No. By the time that a patient becomes ill of a viral infection most of the cells of that patient which are going to be infected have already become infected by the virus producing the illness. Since antibodies do not get into cells the administration of convalescent serums at this time as a rule cannot do a great deal of good.

ANTIBIOTICS AND THE COMMON COLD

QUESTION (Dr. H. Morrison, Boston): Is it worth while giving antibiotics in the common cold or influenza?

ANSWER: No.

RICKETTSIAL DISEASE

QUESTION: What is the mechanism of para-aminobenzoic acid in rickettsial disease?

ANSWER: The mechanism of the action of this drug in rickettsial diseases is not known. It is considered to influence the host cell in some manner so that the rickettsias cannot multiply. In any event, the action does not seem to be against the rickettsias themselves.

NUTRITIONAL CONTROL OF VIRAL DISEASES

QUESTION: Is it feasible to attack viral disease by nutritional control or does it take too long to bring about such influences?

ANSWER: To influence the course of most viral diseases by means of ordinary nutritional control would take too long to be of practicable value. On the other hand, it might be feasible to alter some special enzymatic or metabolic process of host cells sufficiently rapidly to influence favorably the outcome of certain viral and rickettsial diseases. Several investigators are working in this direction.

RECENT ADVANCES IN TREATMENT IN FIELD OF GASTROENTEROLOGY

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Philadelphia

In the allotted time it is not possible to review all the recent therapeutic advances in the field of gastroenterology. I shall confine my remarks to those topics which have attracted most attention in both medical and lay literature. Perhaps in the question and answer period time may be afforded for discussion of other topics.

PSYCHOSOMATIC ASPECTS

A large number of patients presenting themselves to the internist and to the general practitioner for relief of gastrointestinal complaints have no recognizable organic disease in the alimentary tract or elsewhere. Furthermore, although proof is lacking to support the psychogenic origin of common gastrointestinal disorders like peptic ulcer, regional enteritis and ulcerative colitis, a careful psychologic survey on many of these patients is highly suggestive of the presence of an important psychogenic component in their illness. Weiss [1] stated, "Psychosomatic disturbances of gastrointestinal function occur in healthy people subjected to unusual emotional stress and disturbances of gastrointestinal function are among the commonest manifestations of emotional stress in neurotic people." I believe that these statements can be accepted in full and that, among some of the older physicians trained only along organic lines, too little attention is devoted to an appraisal of emotional factors in gastrointestinal disorders. The statement was made by Alvarez,[2] "Every gastro-enterologist who hopes to be worthy of his name and would like to cease making one serious blunder after another should be learning all he can about the psychiatry of the apparently sane. Like me, he may not have wanted to get into this field of medicine but he cannot stay out of it and be a safe internist." It is hoped that the next generation of internists will be sufficiently trained in psychiatry to appreciate the importance of psychic components in illness and that the well trained psychiatrist will continue to insist on the elimination of organic disease before concluding that the psyche is all important. This situation will exist only when the preliminary training of the psychiatrist includes training in internal medicine and when the internist by training has become something of a psychiatrist. Certainly the gastrointestinal internist to be a successful therapeutist must appreciate the significance of emotional factors and the part such factors play not only in functional but in organic disorders as well.

CARCINOMAS OF ESOPHAGUS AND CARDIAC END OF STOMACH

Approximately 2,000 persons die in the United States every year of carcinoma of the esophagus.[3] In 35 to 50 per cent of cases, the lesion is located in the lower end of the esophagus.[4] There is some statistical evidence to suggest that distant metastasis is absent in 25 to 40 per cent of patients who succumb as a result of carcinoma of the lower portion of the esophagus.

Approximately 10 per cent of carcinomas of the stomach occur in the cardiac end.[4] Many neoplastic lesions in this region eventually extend into the lower part of the esophagus. Until recently patients with carcinoma of the lower part of the esophagus and of the cardiac end of the stomach have been regarded as having an almost hopeless prognosis, and in most instances operation was not attempted. As a result of advances in thoracic surgery and in anesthesia, together with the widespread use of chemotherapeutic agents, resection and immediate restoration of continuity have become a possibility in many patients having lower esophageal and high gastric neoplasms. By means of the transthoracic approach a number of surgeons are now resecting the lower part of the esophagus or the lower part of the esophagus and the upper part of the stomach and reestablishing continuity by doing an esophagogastrostomy in the treatment of these lesions.[5]

An expertly trained surgeon is capable of exploring the lower part of the esophagus by the transthoracic approach with an insignificant mortality. Recently Clagett reported twenty-four explorations of this type in which the lesions were found to be inoperable without a single mortality. At the Graduate Hospital, Hawthorne [6] has opened and closed the thorax for inoperable carcinoma of the lower part of the esophagus in 3 instances without a mortality. What is the anticipated mortality when the lesion is resected? The immediate postoperative mortality in Clagett's series of 27 cases of transthoracic resection of the cardia and lower portion of the esophagus was approximately 19 per cent. The mortality in the large group of patients operated on by Sweet is now somewhere between 12 and 15 per cent. Hawthorne [6] at the Graduate Hospital attempted transthoracic esophagectomy (lower part of the esophagus) sixteen times within the past year and a half. In 3 instances the lesion was not resectable. Three of the 16 patients died in the immediate postoperative period; 3 other patients died within two to four months; 7 patients are living from three to fifteen months after operation. It now seems obvious that some patients with carcinoma of the lower part of the esophagus and of the cardiac end of the stomach may be cured by radical transthoracic resection. It is quite possible that the five year cure rate may be as high as or higher than that encountered in radical resection for carcinoma at the lower end of the stomach. The perfection of the technic of partial esophagogastrectomy by the transthoracic approach represents a definite advance in the treatment of carcinoma in this region. Obviously every large medical center should include in its personnel a surgeon who is expert in the performance of these operations.

AMINO ACIDS IN DIET OF PATIENT WITH ULCER

In 1942 Levy and Siler [7] demonstrated the buffering effect of a pancreatic enzymatic hydrolysate of casein on gastric acidity. The introduction of 30 Gm. of the

Read in a Panel Discussion on Recent Advances in Treatment before the joint meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 13, 1947.

1. Weiss, E., and English, O. S.: Psychosomatic Medicine, Philadelphia, W. B. Saunders Company, 1943.
2. Alvarez, W. C.: Nervousness, Indigestion and Pain, New York, Paul B. Hoeber, Inc., 1943.
3. Hoffman, F. L.: Cancer of Esophagus, New England J. Med. **211**: 769-772 (Oct. 25) 1934.
4. Clagett, O. T.: Transthoracic Resection of Lesions of the Lower Portion of the Esophagus and the Cardia of the Stomach, Proc. Staff Meet., Mayo Clin. **20**: 506-507 (Dec. 26) 1945.
5. Churchill, E. T., and Sweet, R. H.: Transthoracic Resection of Tumors of the Stomach and the Esophagus, Ann. Surg. **115**: 897-920 (June) 1942.
6. Hawthorne, H.: Personal communication to the author.
7. Levy, J. S., and Siler, K. A.: Clinical Studies of Amino Acids: Effects of Oral Administration of Solution of Amino Acids Mixture on Gastric Acidity, Am. J. Digest. Dis. **9**: 354-356 (Oct.) 1942.

amino acid mixture into the stomach caused a disappearance of hydrochloric acid in the majority of normal subjects for thirty to forty minutes. These workers suggested that amino acid mixtures might prove of benefit in the management of peptic ulcer. Co Tui and his associates [8] (1945) reported their experience with "hyperalimentation treatment" of peptic ulcer, employing feedings of protein hydrolysates and "dextri-maltose." They stressed the value of this method in healing active ulcers previously thought to be intractable. The efficiency of the method was attributed to the buffering action of the protein hydrolysate and the alleviation of a protein deficiency presumed to be present in many of their patients. These workers deserve credit for drawing the attention of the clinician to the value of high protein feedings in the management of the patient with ulcer who is undernourished. Unfortunately, in the lay press the method was described as a new cure for peptic ulcer, and many patients have been unnecessarily subjected to the ingestion of unpalatable mixtures of amino acids as a substitute for more orthodox and usually equally efficient ulcer regimens.

Briefly, the facts concerning the usefulness of an amino acid diet formula in the treatment of active peptic ulcer are as follows:

1. The buffering action of the amino acid mixture under discussion is not uniform in all patients and the antacid value of many of the newer hydrolysates remains to be tested. There is no proof at hand to indicate that the buffering action of the protein hydrolysate administered every two hours as originally advocated by Co Tui is superior to or even as efficient as the neutralization of gastric acidity which is accomplished by the orthodox ulcer management (hourly feedings of milk, nonsoluble antacids hourly and vagus depressants). In a recent publication, Co Tui and Garcia [9] stated that it became necessary to administer the hydrolysate mixture more frequently (thirty minutes to one and one-half hours) in order to obtain prompt relief of pain in many patients. Six of 23 patients treated by the Co Tui plan by Hodges [10] required feedings more frequently than each second hour for the first few days.

2. Little is known at present of the secondary gastric secretagogue effect of various amino acid mixtures now commercially available.

3. The concept that most patients with uncomplicated peptic ulcers have a protein deficiency has not been proved. Certainly the average private patient seen in the physician's office usually shows no measurable evidence of such deficiency.

4. No objective evidence has been offered to indicate that protein hydrolysates cause any more rapid healing of a gastric or duodenal ulcer than the orthodox feeding mixture of milk (hourly) with the nonabsorbable antacids and vagus depressants.

5. The original protein hydrolysate employed by Co Tui is so unpalatable that many patients are unable to take it without disagreeable side effects (nausea, anorexia and diarrhea).

A perusal of recent publications dealing with amino acid mixtures as the keystone for treatment of active peptic ulcer supplies no convincing evidence of their superiority over milk formulas in the well nourished patient.[11] There is every reason to believe that reliance on these mixtures alone and ignoring of the many items utilized by the experienced gastroenterologist in all-out therapy is unfortunate.

HORMONE THERAPY IN PEPTIC ULCER

Two hormones, elaborated in the body, when injected into Mann-Williamson dogs have proved most successful in the prevention of peptic ulcer, which ordinarily occurs in approximately 98 per cent of animals so prepared.[12] One of these hormones is enterogastrone, a chalone which is released by contact of the intestinal mucosa with fat. By chemical fractionation, extracts of intestinal mucosa have been prepared by Ivy and his associates.[13] These extracts containing enterogastrone, when injected intravenously, inhibit gastric secretion and motility, thus simulating the action of endogenously released enterogastrone. Recently Ivy and Grossman have reported the results of the daily parenteral administration of enterogastrone in dogs prepared with the Mann-Williamson operation. In 76 per cent of the dogs an ulcer did not develop during the first year after operation. In similarly operated animals, not protected with enterogastrone, death occurred on an average of 3.8 months after operation. Treatment was discontinued in 28 Mann-Williamson animals that remained alive after having had enterogastrone injections for one year. In only 2 of these dogs did ulcer subsequently develop, at eighteen and twenty-eight months after cessation of treatment. Twenty-six of the animals survived from eleven to sixty months after therapy was stopped, dying of causes other than ulcer.

A second hormone (urogastrone), recovered from urine, when injected into the experimental Mann-Williamson animal, has an effect rather similar to that of enterogastrone on gastric acidity and motility.[14] This material contains an element called anthelone (anti-ulcer) by Sandweiss, which when injected parenterally also greatly reduces the incidence of experimental ulcer in Mann-Williamson dogs. Furthermore, as with enterogastrone, in the Mann-Williamson animals so treated ulcer failed to develop for long periods of time after the injections of anthelone had been discontinued. Interestingly enough urogastrone is no longer secreted in the urine after hypophysectomy, indicating that the pituitary gland is in some way concerned with its manufacture.[14] It is not known at present whether enterogastrone and urogastrone are the same substance; indeed, neither of them has been crystallized.

Ivy and his associates have treated 27 patients with chronic peptic ulcer by intramuscular injection of 200 mg. of intestinal extract containing enterogastrone.

8. Co Tui; Wright, A. M.; Mulholland, J. H.; Galvin T.; Barcham, I., and Gerst, G. R.: Hyperalimentation Treatment of Peptic Ulcer with Amino Acids (Protein Hydrolysate) and Dextri-Maltose, Gastroenterology **5**: 5-17 (July) 1945.

9. Co Tui and Garcia, E.: The Hyperalimentation Treatment of Intractable Peptic Ulcers with Protein Hydrolysates in Modern Management of Gastro-Intestinal Disease, Philadelphia, J. B. Lippincott Company, to be published.

10. Hodges, H. H.: Protein Hydrolysate Therapy for Peptic Ulcer, Gastroenterology **8**: 476-493 (April) 1947.

11. Hodges [10] tried the Co Tui plan in 26 patients. Three obtained no symptomatic relief. There was no roentgen evidence of improvement in 3 other patients (operation was required). Five of the remaining 20 patients with roentgen evidence of improvement had a recurrence of symptoms within one to five months after termination of therapy. Only 14 patients remained asymptomatic for one to eight months.

12. Ivy, A. C., and Grossman, N. I.: Present Status of Enterogastrone in the Therapy of Peptic Ulcer, Philadelphia, J. B. Lippincott Company, to be published.

13. Greengard, H.; Atkinson, A. J.; Grossman, M. I., and Ivy, A. C.: The Effectiveness of Parenterally Administered Enterogastrone in the Prophylaxis of Recurrences of Experiment and Clinical Peptic Ulcer, Gastroenterology **7**: 625-649 (Dec.) 1946.

14. Sandweiss, D. J.: Enterogastrone, Anthelone and Urogastrone, Gastroenterology **5**: 404-415 (Nov.) 1945.

dissolved in 4 cc. of water, six days a week. This treatment was continued for one year in 18 patients, and in 9 patients the injections were given for periods of five to ten months. In the first group 5 patients had recurrences during the treatment and 2 additional patients experienced recurrences after treatment had been discontinued—a total of 7 patients with recurrences among 18 patients treated. The authors considered this record to be much better than the anticipated results from ordinary clinical management of ulcer without enterogastrone injection, estimating that 60 per cent of patients may be expected to suffer relapses within two years after ordinary medical management. Their incidence of relapses was 39 per cent of 18 patients who had been under treatment for one year. Ivy and Grossman considered their experience as suggestive at least that intestinal extracts containing enterogastrone may prove beneficial in the prevention of recurrences in patients with peptic ulcer disease. Obviously the series of cases is too small and the follow-up too short as yet to come to a more definite conclusion. Ivy and his associates [15] have recently stated that the oral administration of a crude extract of intestinal mucosa prevented ulcer from occurring in 75 per cent of 20 Mann-Williamson dogs and that when this treatment was discontinued the surviving animals failed to have ulcer in most cases. Up to this time there are no records of a large series of patients treated by oral administration of extracts containing enterogastrone with an adequate follow-up.

Sandweiss and his group have also been treating patients with antiulcer factors (anthelone) contained in urine extracts and have reported encouraging preliminary results. They warned against premature optimism, indicating that more purified and more concentrated extracts are needed and that a larger series of patients must be treated and observed over a long period of time before an accurate appraisal can be had. Up to this time no evidence has been forthcoming to indicate that hormones will prove of great value in the healing of ulcer. If they are to have any value in ulcer disease, evidently it will be in the prevention of recurrences.

SECTION OF THE VAGUS NERVES

How Commonly Should Vagus Interruption Be Employed in the Treatment of Peptic Ulcer Even If Its Efficacy Were Proved?—In most patients with uncomplicated duodenal [15] ulcer (probably 60 per cent) an adequately arranged medical regimen results in satisfactory relief (five years or longer). Another 25 per cent have recurrences which can be satisfactorily controlled without significant economic loss or prolonged discomfort. In approximately 10 to 15 per cent the results are unsatisfactory because of obvious complications or intractability. It is only in this latter group that surgical procedures of any kind are considered. In a large number of these because of obstruction or plastering of the ulcer, vagotomy alone should not be undertaken. By these criteria, section of the vagus fibers might come up for consideration in approximately 5 per cent of ulcer patients not operated on. This would comprise almost entirely those ulcer sufferers who have strongly positive insulin reactions, whose attacks seem related to emotional incidents and those who, in spite of a thorough understanding of the total ulcer problem, are unable to avoid severe recurrences. Even though vagus section accomplished the results expected of it, it should never be recommended until adequate medical therapy, including attention to all known etiologic factors, has been given a thorough trial—if for no other reason than the present known record that the most sanguine statistics indicate results satisfactory to the patient in not more than 80 per cent. It is unfortunate that the criteria mentioned here were not fulfilled in many instances before vagus section was so frequently performed in many clinics.

What Is the Rationale of Vagus Section for Peptic Ulcer?—It was hoped that a severance of nervous pathways between the brain and stomach would: (1) effectively abolish the cephalic phase of gastric secretion (Pavlov's experiments reported in 1910 [16] proved that the vagus nerves in the dog are the pathways for the stimuli which excite the psychic phase of gastric secretion); (2) reduce or abolish excessive interdigestive and night secretion of hydrochloric acid in the stomach; (3) reduce excessive motor activity of the stomach and duodenum; (4) abolish the harmful effects on the gastric circulation which might be of emotional origin (color changes in the gastric mucosa due to vascular congestion induced by resentment and anger were noted by Stewart Wolf [17] prior to a vagotomy but did not occur after vagus section in a patient operated on by Andrus), and, (5) as a result of these effects on the stomach, encourage healing of active ulcer and prevent recurrences.

How Complete Must Vagus Denervation of the Stomach Be in Order to Accomplish These Anticipated Results?—It has been shown repeatedly in both animals and man that the desiderata which have been set forth may not be accomplished unless all the vagus fibers are interrupted (however, an inhibiting effect on gastric secretion and motility has been reported in some instances when the vagus denervation of the stomach has not been complete). It was in order to accomplish complete vagus denervation of the stomach that Dragstedt adopted the operation of supradiaphragmatic vagotomy.

Is Complete Interruption of the Vagus Fibers to the Stomach Always Possible?—Evidently complete interruption is not possible. Those students who have closely studied the anatomy of this region point out that variation in the course and number of vagus fibers both above and below the diaphragms is so great that it would be impossible in some instances to interrupt all the fibers.[18]

The accepted test for determining the presence of intact nerve fibers after vagus operations is the insulin test.[19] If this test is used as a criteria of continuity of the vagus, then the most expert surgeon fails to sever all fibers at times even when the operation is

15. Patients with gastric ulcer probably should not be exposed to supradiaphragmatic operations because of the inability to inspect the lesion and excluded carcinomatous ulcer.

16. Pavlov, I. P.: The Work of the Digestive Glands, ed. 2, London, C. Griffin & Co., 1910.

17. Wolf, S., and Andrus, W. D.: The Effect of Vagotomy on Gastric Function, Gastroenterology **8**: 429-434 (April) 1947.

18. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, J. A. M. A. **133**: 459-461 (Feb. 15) 1947. Miller, E. M., and Davis, C. B.: An Anatomic Study of the Vagus Nerves, J. A. M. A. **133**: 461-462 (Feb. 15) 1947. Hawthorne, H.: Personal communication to the author.

19. Weinstein, V. A.; Colp, R.; Hollander, F., and Jemerin, E. E.: Vagotomy in Therapy of Peptic Ulcer, Surg., Gynec. & Obst. **79**: 297-305 (Sept.) 1944. Hollander, F.: The Insulin Test for the Presence of Intact Nerve Fibers After Vagal Operations for Peptic Ulcer, Gastroenterology **7**: 607-614 (Dec.) 1946.

performed by the transthoracic route. Three of 8 patients recently subjected to this operation by Weinstein and Colp [20] had positive insulin reactions after operation (however, these 3 were relieved of pain). I know of no large reported series of cases of vagus section in which the reaction to the insulin test was invariably negative after the operation.

It is this effort to sever all fibers of the vagus going to the stomach which caused surgeons to try the transthoracic approach and which has caused some to prefer actual vagus resection to simple vagotomy.[21] I have stated that the postoperative insulin test is evidently a method of distinguishing between complete and partial vagotomy. One wonders whether the degree of delay in stomach emptying may not also measure to some extent the completeness of the vagotomy. Perhaps those patients who have had the most complete vagotomies are those whose stomachs empty most poorly or not at all after operation. I have 1 patient who was operated on Sept. 14, 1946, who up to this time (May 1947) requires "urecholine" (carbaminoyl-beta-methylcholine chloride) two to three times daily in order to empty his stomach. His reaction to the insulin test is negative; yet the hydrochloric acid titer of his fasting stomach is 90 units if no "urecholine" is taken after supper the night before.

It is because of this unphysiologic side effect of vagotomy (delay in stomach emptying) that Dragstedt and others are now looking with favor on the abdominal approach—infradiaphragmatic vagotomy combined with gastrojejunostomy. Thus the initial thesis, that the transthoracic approach makes it possible to accomplish a more nearly complete vagotomy, is being abandoned in some clinics. In this connection perhaps it should be mentioned that there is no proof that gastroenterostomy will invariably function satisfactorily in the vagotomized stomach. This swinging of the pendulum in some clinics toward the subdiaphragmatic operation would appear to be an admission that the side effects of a complete vagotomy are undesirable. The only other valid conclusion to be drawn from this change of heart would be that the cases selected for the supradiaphragmatic operation were poorly chosen, many with associated obstructive lesions having been included.

Side Effects of Vagus Interruption.—Many physiologically minded clinicians have been concerned about the increased popularity of so-called complete vagotomy in the treatment of peptic ulcer because of possible interference with important functions of the stomach, pancreas, biliary tract and intestines. Many years ago Pavlov noted that complete vagotomy in dogs resulted in a lack of stomach emptying and subsequent death of the animals of subnutrition. Hartzell [22] made no mention of gastric dilatation or faulty nutrition in his vagotomized dogs, but their survival time was not given. Complete vagotomy in rats, according to Shay and Komarov,[23] results in death of the animals within ten days if they are allowed to partake of their stock diet. The stomach and esophagus of these animals were dilated and filled with food residue. It is well to keep in mind the statement of Necheles,[24] "we will have to wait for many years to know the trophic effects of section of the vagi on such organs as the pancreas, the liver, the intestinal mucosa, etc."

There is evidently little risk involved in doing the supradiaphragmatic vagotomy, judging from the reports emanating from many clinics. However, both Weeks and co-workers [25] and Moore and his associates [21] have reported a death, evidently the result of cardiac standstill following vagotomy.

The most important undesirable side effects of vagus section are those due to disturbances in motility of the digestive tract. So-called achalasia or cardiospasm, to be anticipated, has not been reported frequently. Diarrhea may be troublesome. It occurred in 40 per cent of 30 patients reported by Ruffin and Smith.[26] Evidently it was mild and caused little inconvenience. In these same patients gastric motility was profoundly affected by vagotomy in each instance. Peristaltic waves were absent and gastric dilatation occurred. Apparently the tone of the stomach returned toward normal after several months. Subsequent gastroenterostomy or pyloroplasty was required in 3 of the 30 patients subjected to vagotomy by Ruffin and Smith. Many others have had a similar experience. Fortunately Machella and his associates [27] have found "urecholine" effective in increasing gastric tonus and initiating contraction waves in the atonic stomach, the result of vagotomy. The use of the drug has now obviated the necessity of reoperation in a number of instances. Evidently rather often the delay in emptying following vagotomy disappears in several months, and during this time "urecholine" may be used.

Dorsolumbar sympathectomy for hypertension should not be performed in patients who have had peptic ulcer. Blegen and Kintner [28] reported a patient who suffered three severe hemorrhages from a prepyloric ulcer following this operation, who was subsequently subjected to subtotal gastrectomy. Weeks and co-workers [25] performed a transthoracic vagotomy for duodenal ulcer and a left thoracolumbar sympathectomy for hypertension. The ulcer pain was relieved. However, fifteen days after the second stage right thoracolumbar sympathectomy, the patient died of perforation of the duodenal ulcer without having experienced pain.

An Appraisal of Results of So-Called Complete Vagotomy.—1. The cephalic phase of gastric secretion measured by the insulin test,[29] by sham feedings and by reduction in volume of night secretion [29a] is either abolished or greatly diminished by intrathoracic vagotomy. The secretory response to insulin if abolished by the operation remains absent at the end of a year.[21] However, even now there are too few published reports of satisfactorily performed insulin tests late after vagotomy to indicate that the reaction to the insulin test will remain permanently negative. It should be recalled

20. Weinstein, V. A., and Colp, R.: Supradiaphragmatic Vagotomy in Gastrojejunal Ulceration Following Subtotal Gastrectomy for Duodenal Ulcers, S. Clin. North America **27**: 249-253 (April) 1947.

21. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**: 241-251 (Feb. 21) 1946.

22. Hartzell, J. B.: The Effect of Section of the Vagus Nerves on Gastric Acidity, Am. J. Physiol. **91**: 161-171 (Dec.) 1929.

23. Komarov, S. A., in discussion on Symposium on Peptic Ulcer with Particular Reference to Vagotomy, Gastroenterology **7**: 620 (Dec.) 1946.

24. Necheles, H., in discussion on Symposium on Peptic Ulcer with Particular Reference to Vagotomy, Gastroenterology **7**: 622 (Dec.) 1946.

25. Weeks, C.; Ryan, B. J., and Van Hoy, J. M.: Two Deaths Associated with Supradiaphragmatic Vagotomy, J. A. M. A. **132**: 988-990 (Dec. 21) 1946.

26. Ruffin, J. M., and Smith, R. C.: The Treatment of Peptic Ulcer with Special Reference to Vagotomy, Am. Pract. **1**: 118-120 (Nov. 1) 1946.

27. Machella, T. E.; Hodges, H. H., and Lorber, S. H.: The Restoration of Gastric Motility by Urethane of B-Methyl Choline After Section of the Vagus Nerves for Peptic Ulcer, Gastroenterology **8**: 36-51 (Jan.) 1947.

28. Blegen, H. M., and Kintner, A. R.: Aggravation of Gastric Ulcer Following Dorsolumbar Sympathectomy, J. A. M. A. **133**: 1207-1209 (April 19) 1947.

29. (*a*) Thornton, T. F., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves, J. A. M. A. **130**: 764-771 (March 23) 1946. (*b*) Grimson, J. S., in discussion on Thornton,[29a] p. 769. (*c*) Moore, Chapman, Schulz and Jones.[21]

that postprandial acidity is rarely abolished by this operation, as it is so frequently after large subtotal gastrectomy performed for peptic ulcer. The gastric secretory response to histamine and to caffeine is unaffected. Consequently, if in many instances of peptic ulcer the initiating influence is not vagal in origin, the vagotomy cannot be expected to prevent recurrences.

2. The decreased tonus and diminished amplitude of contractions of the stomach wall, noted invariably after complete vagotomy, are evidently not always lasting. The motor activity of the resting stomach was practically normal one year after operation in the patients of Moore and his colleagues. Furthermore, the extreme delay in stomach emptying experienced by many patients after intrathoracic vagotomy gradually disappears after several months, according to most observers (however, 1 of my patients must take "urecholine" daily, eight months after intrathoracic vagus resection, in order to empty his stomach and maintain normal nutrition [30]). Obviously, as stated by Moore and co-workers, if interruption of the vagus nerves is to have a lasting effect in the prevention of recurrences of ulcer, this effect cannot be related to changes in fasting acidity or gastric motility.

3. Perhaps any lasting benefit which is to be derived from this operation may depend on an interruption of those cephalic impulses caused by emotional incidents which give rise to vascular change in the stomach (observation of Stewart Wolf [17] previously cited). It remains to be seen whether this observation of Wolf will be borne out by further study and, if so, whether the desired absence of such vascular change in the mucosa of emotional origin will be permanent.

4. All observers have agreed that relief of pain is usually prompt and all evidence suggests that active ulcers usually heal promptly after intrathoracic vagotomy. It is of interest that relief of pain is not always dependent on an absence of interdigestive or cephalic gastric secretion and does not always depend on a severance of all vagus fibers (observation of Weinstein and Colp [20] previously mentioned). Pain initiated by an appropriate gastric stimulus can be experienced by the patient after vagotomy if a dorsolumbar sympathectomy has not been performed.

The citation of all observers that relief of pain is immediate is not the important issue here. Ulcer pain in many of these patients could have been promptly relieved by a medical regimen, including hourly feedings, atropinization and antacids. Our concern is with prevention of recurrence and cure of the disease. Recurrences of ulcer are being reported following intrathoracic vagotomy; yet up to this time they have not exceeded 10 per cent of patients subjected to operation. Too little time has elapsed to be able to state what the ultimate results will be so far as the cure of ulcer is concerned. It is clear, however, that the rate of cure will not approach 100 per cent, and it is doubtful whether the results will be any better than or as good as an expertly performed high subtotal gastric resection with or even without an infradiaphragmatic partial vagotomy.

SUMMARY

I believe that the operation of complete intrathoracic vagus interruption or resection remains an experimental procedure. A complete interruption of the vagus innervation of the stomach is not always possible, and it may yet prove to be undesirable because of late side effects. Until the final results of adequate follow-up are available it should not be undertaken lightly in the patient who has not been operated on. Only patients with duodenal ulcer who have a strongly positive reaction to the insulin test and a history suggesting emotional influences in the initiation of attacks and who have not responded to really adequate medical treatment should be considered as candidates for the experiment. Gastric ulcer or delay in stomach emptying in duodenal ulcer should be looked on as contraindications. The operation should be undertaken only by surgeons thoroughly experienced in the procedure. It is not without danger. At this time, I believe that intrathoracic vagotomy can be considered the operation of choice only in those patients who have experienced recurrence of ulcer after a large subtotal gastrectomy which has included ablation of the antral and pyloric mucosa.

NOTE:—One year after vagus resection stomach emptying has improved sufficiently to permit of discontinuance of "urecholine."

30. See note at end of paper.

ABSTRACT OF DISCUSSION

ULCERATIVE COLITIS

QUESTION: Are antibiotics useful in the treatment of chronic ulcerative colitis?

ANSWER: Most clinicians have had little success with the use of antibiotics in the chronic stage of chronic ulcerative colitis. Occasionally, a remission has been experienced during the course of administration of penicillin and of streptomycin, but in these instances there is little proof to indicate that the improvement may not have been dependent on comprehensive therapy including mental and physical rest, rather than on the so-called specific agent. Some clinicians have reported good results in the treatment of the acute fulminating febrile type of ulcerative colitis. One of these is Dr. Burrill Crohn, who administered 0.5 Gm. of streptomycin by mouth and 0.5 Gm. intramuscularly every six hours for forty-eight hours. Others have reported improvement in acute fulminating ulcerative colitis which seemed to be related to the administration of penicillin. I have had this experience in a few instances. Certainly, these agents should be tried, particularly in the fulminating stage of the disease, but all other methods of therapy should be included in the regimen with particular emphasis on the maintenance of good nutrition.

VAGOTOMY AND DUODENAL ULCER

QUESTION: Is vagotomy a satisfactory surgical treatment of simple duodenal ulcer with intractable pain?

ANSWER: I do not believe that complete vagotomy alone can be looked on as satisfactory surgical treatment for duodenal ulcer in most instances. My experience has been that if surgical treatment is necessary in duodenal ulcer, complications, particularly that of plastering of the ulcer, necessitate the more radical, large, subtotal gastrectomy. My present feeling about vagotomy is discussed in some detail in the paper.

ANTACIDS

QUESTION: What are the most effective antacids?

ANSWER: Antacids have a place in the management of many patients with peptic ulcer disease; they may be divided into (1) soluble antacids and (2) nonabsorbable antacids. The former group are not utilized to the point of causing complete neutralization of gastric acidity by most gastroenterologists today. They have lost favor because of their tendency to encourage the development of alkalosis, on one hand, and because of their secondary gastric secretory effect, on the other. However, a combination of soluble antacids including calcium carbonate, magnesium oxide and sodium bicarbonate every third or fourth hour in the active stage of ulcer management often works well.

Nonabsorbable antacids are more popular at present. In this group, perhaps one could include the newer anion exchange resins and the detergents (sodium alkyl sulfate). Theoretically both of these groups of substances perhaps have the advantage of buffering the acid and reducing the peptic activity and perhaps even encourage the stimulation of mucin without having any secondary gastric secretory effect or any deleterious effect on the acid-base balance of the blood. However, insufficient clinical trials have been reported to justify the widespread use of these substances until certain disadvantages have been overcome. The most widely used nonsoluble antacids remain aluminum hydroxide gel, aluminum phosphate gel and magnesium trisilicate. The combination of magnesium trisilicate and aluminum hydroxide prepared in tablet form by several manufacturers has proved efficient in treatment of my patients.

RAPID EMPTYING OF STOMACH

QUESTION (Dr. Joseph Bank, Phoenix, Ariz.): What can be done to relieve symptoms due to rapid emptying of the stomach after partial gastrectomy?

ANSWER: This is a very difficult question because, in the first place, one must know why the stomach is emptying too rapidly, and in many instances it is the result of an improperly performed gastrectomy. Usually, I have adopted the plan of continuing the patient on frequent feedings of rather small quantities containing a rather large amount of fat, preferably in the form of cream. Furthermore, large doses of atropine or belladonna may be of benefit in these cases. Of course, in some instances some thought might be given to the gastrogenous type of diarrhea by the administration of appropriate doses of hydrochloric acid. I think that type of treatment should be held in abeyance until the dietary plan and antispasmodics have been utilized.

CURE OF PEPTIC ULCER

QUESTION (Dr. J. R. Bleich, Atlanta, Ga.): Do you think it likely that any one procedure will ever suffice to cure peptic ulcer? Or do you believe that treatment will have to be continuous throughout the life of the patient?

ANSWER: To answer this question adequately would require one hour. First, one must define what is meant by "cure." If one means the failure of slight epigastric distress to appear at any time in the future following adequate medical therapy, then one could say that perhaps not more than 25 per cent of patients with duodenal ulcer are cured by medical management. However, more nearly 75 per cent of patients who are adequately treated medically for duodenal ulcer, including advice for the prevention of recurrences, remain sufficiently well so that they suffer no economic loss and are soon relieved of their recurrences of minor distress by resuming at once a strict regimen for a brief period of time. Many of these patients can lead a fairly normal life providing they are alerted to the necessity of resuming a strict regimen at the very beginning of a recurrence.

Subtotal gastrectomy adequately performed by an expert has resulted in a large percentage of so-called five year cures, and many of these patients are leading normal lives. I think that it should be remembered that only about 10 per cent of patients with peptic ulcer disease get into really serious difficulty so as to require major operations. At this writing there is no therapeutic agent which offers a guarantee against recurrence of ulcer even though it be continued throughout life.

ENTEROGASTRONE

QUESTION: Please explain in what way enterogastrone affects healing of the ulcer? Why is it called a hormone?

ANSWER: I know of no proof that the administration of enterogastrone does affect the healing of an individual peptic ulcer. We have experimental evidence to suggest that injections of this material prevent the recurrence of experimental peptic ulcer in the Mann-Williamson animal and that, in addition for a year or more after the discontinuance of the injections of enterogastrone the animal is protected against the development of peptic ulcer. In those few clinics where the material has been used in the treatment of active ulcer, the evidence does not suggest that the material has any remarkable effect on the healing of a particular ulcer. Both enterogastrone and urogastrone when injected parenterally into the animal inhibit gastric secretion and motility, and it is possible that some element in the crude extract may beneficially affect the gastric mucosa and encourage healing; the proof is not at hand up to this time. In referring to the question related to terminology, if "hormone" is used in its strict sense as a substance which is excitatory, then perhaps it should not be applied to enterogastrone, which is really a chalone; i. e., an internal secretion which depresses activity.

HYPERTENSION AND VAGOTOMY

QUESTION (Dr. Morris J. Levine, Miami Beach, Fla): Does hypertension constitute a serious contraindication to vagotomy?

ANSWER: I think that one might safely say that a bilateral dorsolumbar sympathectomy may well have a deleterious effect on the patient with peptic ulcer if for no reason other than the fact that ulcer pain would not be experienced unless the serosa was involved. Ulcer complications have been reported in several cases in which both vagotomy and bilateral dorsolumbar sympathectomy have been performed on the same patient. I am not sure that proof is at hand that severance of the vagus fibers has an unfavorable effect on patients with hypertension, although theoretically one might consider that possibility. I do believe that the risk of complete intrathoracic vagotomy might be increased in patients with hypertension.

HYDROCHLORIC ACID AND PEPTIC ULCER

QUESTION (Dr. Meyer Golob, New York): Has not too much emphasis been placed on hydrochloric acid in the genesis of peptic ulcer? What about the cases of hyperchlorhydria in which ulcer does not develop and the cases of achlorhydria—admittedly ulcers develop in a small percentage? Surely vagotomy should not be singled out as the only agent to combat postoperative hypersecretory activity.

ANSWER: Obviously, hyperchlorhydria alone does not cause peptic ulcer. The hydrochloric acid and pepsin can be looked on only as the attacking force when the antiulcer factors normally present have been weakened or removed. It is true, however, that most clinicians believe that peptic ulcer cannot develop in the stomach which is incapable of secreting hydrochloric acid. I personally know of no authentic instance of active peptic ulcer in a patient who had consistently a histamine-refractory achylia gastrica.

VAGOTOMY

QUESTION (Dr. Albert M. Yunich, Albany, N. Y.): What has been your personal experience with vagotomy? In the light of present knowledge, when do you recommend vagotomy?

ANSWER: That is an embarrassing question, because up to this time I have considered that vagotomy alone, when the patient has not previously had a gastrectomy, is an experiment. Three of my patients have been subjected to intrathoracic vagotomy, and 1, after operation, had a positive reaction to the insulin test and subsequently had a recurrence of ulcer symptoms, at the end of three months. The second patient was operated on last September, and the stomach has never emptied without the aid of "urecholine" since the date of that operation. His reaction to the insulin test remains negative. He is being kept as an experimental guinea pig, with his consent, because most persons believe that the motor-emptying function improves after vagotomy after a period of three, four, five or six months. It is now nine months and there has been no improvement (see note, page 297, at end of paper). The third patient has had a satisfactory result. He had a large subtotal gastrectomy, at which time the pylorus and the mucosa had also been removed. He returned with a gastroduodenal ulcer and has had a complete relief of symptoms which is now of six months' duration.

At present, I should not recommend intrathoracic vagotomy in the treatment of peptic ulcer unless the patient had previously had a large subtotal gastrectomy and unless a gastrojejunal ulcer had developed. A decision has not yet been reached concerning how many patients should have vagotomy combined with other types of gastric operation, such as gastroenterostomy or subtotal gastrectomy. It will require two

or three years before it is known just how valuable this additional procedure of vagotomy may be in the management of peptic ulcer disease, in my opinion.

USE OF HISTAMINE IN PEPTIC ULCER

QUESTION: Have you any opinion on the use of histamine in peptic ulcer?

ANSWER: I have an opinion but it is probably valueless because I have had no experience. It would not be the type of substance that I should be inclined to use in the management of peptic ulcer because of its great stimulating effect on gastric acidity.

PROTEIN HYDROLYSATES

QUESTION: Woolley has stated that the regeneration and growth factors of protein hydrolysate are not found in acid hydrolysates. Enzymatic protein digests, he said, depend on their strepogenin content, which is estimated by its ability to stimulate Lactobacillus casei. The physician cannot at present tell a good hydrolysate from a poor one. Do you not think that if a poor enzymatic protein digest is used the increase in oxygen-carrying power of blood is important? Toxic protein destruction present in neurocirculatory asthenia and duodenal and peptic ulcer is stopped and cured by enzymatic protein digests containing strepogenin.

QUESTION (Dr. H. N. Vermilye, New York): Why criticize protein hydrolysates which do not come up to Woolley's standard? Enzymatic protein digests, according to Woolley, depend on their strepogenin factor, which is measured by stimulation of Lactobacillus casei. Streptogenin factor stimulates protein synthesis from amino acids supplying this factor in toxic protein destruction—supplies a deficiency found in cases in which digestive ability cannot supply it.

ANSWER: My opinion concerning the value of protein hydrolysates in the management of peptic ulcer has been covered in the paper.

ADDITIONAL SURGICAL PROCEDURES

QUESTION (Dr. Emanuel Deutsch, Boston): Are additional surgical procedures such as posterior gastroenterostomy of benefit in recently vagotomized patients for uncomplicated duodenal ulcer when symptoms of delayed emptying time of stomach are predominant?

ANSWER: Additional surgical procedures have been used, in many instances, to overcome the delayed emptying time of the stomach following vagotomy. So far there are insufficient reports in the literature to pass judgment on the efficacy of gastroenterostomy performed for this purpose; evidently it does prove adequate in relieving the gastric stasis in many instances. However, it is highly likely that in some vagotomized stomachs even gastroenterostomy will not result in satisfactory stomach emptying. At present it seems advisable to use "urecholine," as recommended by Machella, to overcome the gastric stasis following vagotomy. This drug evidently works splendidly, and in some instances after some months the motor function of the stomach may improve sufficiently so that a subsequent drainage operation may not be necessary.

VALUE OF LIPOCAIC

QUESTION (Dr. S. J. Rugel, Philadelphia): Is lipocaic of any value in cases of hypertrophy of the liver associated with high blood fats?

ANSWER: Dragstedt and his co-workers have described two types of fatty infiltration, occurring in association with diabetes. One was attributed to uncontrolled diabetes, being characterized by a high blood lipid concentration, acidosis and relief by insulin. In the other form a low blood lipid concentration was noted, associated with impaired hepatic function, decreased secretion of dextrose and increased sensitivity to insulin. This latter type of change was relieved by lipocaic and not by insulin. I have had no experience with the use of lipocaic in cases of hypertrophy of the liver presumed to be the result of fatty infiltration, associated with high blood fats. Theoretically one would expect some benefit from the use of lipotrophic substances in conjunction with a diet high in protein and low in fat.

RECENT ADVANCES IN THE TREATMENT OF CARDIOVASCULAR DISEASE

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Advances in the treatment of heart disease rarely can be referred to any one year. Rather they represent increments of knowledge accumulated over many years. While the treatment of cardiovascular disease is ever progressing, the efficacy of certain advances has been sufficiently well established to warrant mention of them in this summary. In recent years an encouraging number of successful procedures in the treatment of heart disease have been devised which constitute real advances.

CONGESTIVE HEART FAILURE

Digitalis.—It is customary to standardize preparations of digitalis in terms of cat units, a unit being defined as the dose of the drug that is lethal for cats. It is unfortunate that glycosides of digitalis are tested for potency by intravenous administration whereas oral administration is more common when they are used clinically. Gold [1] has shown that among preparations of digitalis there is a great variation in the degree of absorption. Whereas only about 20 per cent of preparations of the digitalis leaf or of the tincture of digitalis is absorbed in the gastrointestinal tract, practically 100 per cent of digitoxin is absorbed. It is noteworthy that only about 10 per cent of an oral dose of lanatoside C is absorbed by the gastrointestinal tract.

Since oral administration is the route of choice in giving digitalis, it is advantageous to have a drug which is absorbed completely. Digitoxin fulfils this requirement perfectly. It is feasible to administer orally a full digitalizing dose (1.2 mg.) of digitoxin with minimal prospect of gastrointestinal irritation by virtue of the small bulk of the drug required to produce the desired effect. When given orally the quantity of lanatoside C (6 to 10 mg.) or of digitalis leaf (1.2 to 1.5 Gm.) required to produce a similar effect leads to nausea and vomiting before a sufficient amount of these drugs is absorbed to produce a full digitalizing effect. Except in emergencies, it is preferable to administer less than a digitalizing dose initially and to achieve full digitalization gradually by the administration of suitable additional daily doses of digitoxin. In this way one can stop short of producing uncomfortable and sometimes dangerous toxic manifestations.

From these statements it should not be inferred that satisfactory effects of digitalis cannot be obtained by a variety of standard preparations of the drug. However, since there is a variation in the percentage of their absorption by the gastrointestinal tract, a considerable experience with a particular preparation is necessary to use it wisely.

It is seldom necessary to administer digitalis parenterally. If vomiting precludes the administration of the drug by mouth or if the situation is so grave that prompt action is required, then it is justifiable to give

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Read in a Panel Discussion on Recent Advances in Treatment before the joint meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 13, 1947.

1. Gold, H.: Pharmacologic Basis of Cardiac Therapy, J. A. M. A. **132**: 547-554 (Nov. 9) 1946.

a digitalis glycoside by the intravenous route. Since ouabain, when given intravenously, attains its full effect in two hours, it is the preparation of choice for quick action. An initial dose of 0.3 mg. given intravenously may be followed by intravenous injections of 0.1 mg. at intervals of two to three hours until a satisfactory effect has been obtained. It is useful to bear in mind that a dose of 3 to 5 cat units of lanatoside C, "digifolin" or digitoxin will produce a satisfactory effect of digitalis when given intravenously, but the action of these preparations is less prompt than that produced by ouabain when similarly administered.

Mercurial Diuretics.—The congestive heart failure of many patients is not adequately controlled by treatment with digitalis. It is well understood that the administration of mercurial diuretics to such patients is indispensable. It is not so well understood that mercurial diuretics are extremely useful in keeping a patient free of edema. It must be remembered that patients can accumulate 7 to 8 pounds (3.2 to 3.6 Kg.) of fluid before its presence is manifested by edema of the dependent portions of the body or by signs of pulmonary congestion. The patient may be aware of the edema because he notes the onset of dyspnea. It is useful and important to forestall the development or minimize the degree of this edema. To accomplish this, Gold [2] advocated the daily injection of 1 to 2 cc. of a mercurial diuretic. Since such frequent injections are burdensome to both patient and physician and since the injection often may not be needed, some more practical guide to the need for injections of mercurial diuretics should be sought. One method which I have found successful is to instruct the patient to weigh himself daily. Under standard conditions a sudden gain of 2 to 4 pounds (0.9 to 1.8 Kg.) should be a signal for him to report to his physician for an injection of a mercurial diuretic. Under such a plan it has been found that the need for injections of mercurial diuretics varies from three times a week to once in two weeks or longer, and yet the patient is protected from dyspnea or the development of more than a minimal amount of latent edema.

It should be emphasized also that the rigid restriction of salt to 1.5 to 2.0 Gm. daily has greatly diminished the need for the administration of mercurial diuretics in cases of congestive heart failure.

Restriction of Sodium and Allowance of Fluid.—Recently, Warren and Stead [3] found that edema would develop in patients who had recovered from previous congestive heart failure if an excessive amount of salt was added to their diets. Under these circumstances the patients gained weight, the total volume of the blood plasma increased, the concentration of the plasma proteins decreased initially, the hematocrit determinations decreased and all of these events preceded an increase in venous pressure. Whether or not one accepts their interpretation that this failure of the kidney to excrete salt is due to the decreased output of a diseased heart and that this failure constitutes the common mechanism of heart failure, nevertheless it serves to focus attention again on the importance of sodium in the genesis of edema.

Since about the turn of the century it has been known [4] that patients suffering from heart disease excreted sodium poorly and that the blood sodium did not increase. From these observations it was inferred that ingested salt contributed to the edema. Renewed interest in this problem was brought about by the challenging work of Schemm,[5] who advocated a program comprised of a very large allowance of water, a sharp restriction of salt, an acid-ash diet, the use of acid-producing drugs and, occasionally, the supplemental administration of mercurial diuretics in the treatment of refractory congestive heart failure. Further studies [6] have indicated that restriction of salt ingestion to 1.5 to 2.0 Gm. daily is the most essential feature of this program, and in a recent discussion White [7] stated that some patients receiving such an allowance of salt remained free of edema even though their allowance of fluid was low. In a group of patients suffering from congestive heart failure who were kept on a greatly restricted intake of salt, Gorham and his associates [8] studied the diuretic effect of increasing intake of fluid. They found that diuresis was enhanced by increasing the intake of fluid up to 3 L. a day, but beyond that, increasing amounts of fluid did not materially augment the diuresis. This evidence indicates that patients on a diet low in sodium do best when they are allowed to take as much water as they desire, up to 3 L. a day. It must not be forgotten that renal function in heart failure is compromised by a reduced cardiac output and sometimes by intrinsic renal disease. Under these circumstances there may still remain instances in which an intake of fluid in excess of 3,000 cc. daily may be required to secure a satisfactory diuresis.

HYPERTENSION

Diet.—In recent years, Kempner [9] has advocated a diet, which is known as a rice diet, in the treatment of hypertensive states which may or may not be associated with demonstrable nephritis. This diet contains no protein of animal origin and has a content of sodium of 0.15 Gm. daily. Kempner observed objective improvement in about two thirds of the patients suffering from hypertension who were treated with this diet. Objective evidences of improvement included: a significant drop in blood pressure, a decrease in size of the heart, often definite improvement in important electrocardiographic abnormalities, a return to normal values of increased levels of nitrogen and cholesterol in the blood and a definite decrease in the changes in the retinal arteries, which are characteristic of hypertension.

Kempner [10] predicted the beneficial results of this diet on the assumption that hypertension causes impair-

2. Gold, H.: Treatment of Heart Failure, Interne, January 1946, pp. 18-23.

3. Warren, J. V., and Stead, E. A., Jr.: Fluid Dynamics in Chronic Congestive Heart Failure: An Interpretation of the Mechanisms Producing the Edema, Increased Plasma Volume and Elevated Venous Pressure in Certain Patients with Prolonged Congestive Failure, Arch. Int. Med. **73:** 138-147 (Feb.) 1944.

4. Achard, C., and Loeper, M.: Sur la rétention des chlorures dans les tissus au cours de certains états morbides, Compt. rénd. Soc. de biol. **53:** 346-347 (March 23) 1901. Merklen, P.: La rétention du chlorure de sodium dans l'oedème cardiaque, Bull. et mém. Soc. méd. d. hôp. de Paris **20:** 725-731 (June 19) 1903. Widal and Lemierre: Pathogénie de certains oedèmes brightiques.—Action du chlorure de sodium ingéré, ibid. **20:** 678-699 (June 12) 1903.

5. Schemm, F. R.: A High Fluid Intake in the Management of Edema, Especially Cardiac Edema: I. The Details and Basis of the Régime, Ann. Int. Med. **17:** 952-969 (Dec.) 1942; II. Clinical Observations and Data, ibid. **21:** 937-976 (Dec.) 1944.

6. Wheeler, E. O.; Bridges, W. C., and White, P. D.: Diet Low in Salt (Sodium) in Congestive Heart Failure, J. A. M. A. **133:** 16-19 (Jan. 4) 1947.

7. White, P. D.: Unpublished data.

8. Gorham, L. W.; Lester, D. E.; Wolf, A. V., and Shultz, H. B.: The Relative Importance of Dietary Sodium Chloride and Water Intake in Cardiac Edema, unpublished data.

9. Kempner, W.: Compensation of Renal Metabolic Dysfunction: Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet; III., North Carolina M. J. **6:** 61-87 (Feb.) 117-161 (March) 1945.

10. Kempner, W.: Some Effects of the Rice Diet Treatment of Kidney Disease and Hypertension, Bull. New York Acad. Med. **22:** 358-379 (July) 1946.

ment of function of the cells of the kidneys, presumably because the supply of oxygen available to these cells is decreased. As a result, the kidneys are affected by impairment of their capacity to deaminize amino acids, oxidize keto acids and form ammonia, and this failure leads to hypertension. Kempner substituted vegetable for animal proteins on the theory that the injured kidney in hypertension can no longer excrete properly the catabolic products of animal proteins. It has been calculated that 76 per cent of all the work of the kidney is spent on the excretion of urea. The concentration of urea nitrogen in the total volume of urine excreted in twenty-four hours is one fifth less in patients on a rice diet than in those on a starvation diet and, hence, the diet greatly decreases the work of the kidney.

It will be admitted by all that the rice diet is a monotonous diet. Grollman [11] found that the restriction of sodium results in a pronounced decrease in blood pressure in rats in which hypertension had been induced experimentally. Believing that perhaps the restriction of sodium in the rice diet was the essential factor in its beneficial effect on hypertension, this investigator and his associates [12] treated 6 patients who had hypertension by a more general diet containing animal proteins but only 0.5 Gm., or less, of sodium daily. In some of these cases they observed a striking decrease in blood pressure comparable to that observed when the more rigid and monotonous rice diet was used. These observers have not reported the effect of the restriction of sodium on the sodium, potassium, chloride and urea levels in the blood and urine for comparison with the results obtained by Kempner for patients who were treated with the rice diet.

These observations open up a new approach to the treatment of hypertension by dietary measures which deserve further study under carefully controlled conditions. Such studies should provide better agreement on the optimal composition of such a diet and should define its indications and limitations.

SUBACUTE BACTERIAL ENDOCARDITIS

When penicillin was first used in the treatment of subacute bacterial endocarditis, there were so many failures that many clinicians despaired of its usefulness. Further experience has shown that these failures were due almost entirely to insufficient doses of penicillin. The experience of Hunter [13] permitted him to state that "the great majority of patients who have streptococcal endocarditis can be cured with sufficiently intensive administration of penicillin."

Early diagnosis is essential. The disease should be suspected in any patient with valvular heart disease who has unexplained fever for a week or more or who exhibits embolic phenomena, splenomegaly or unexplained anemia.

It is useful to establish the sensitivity of the infecting organism to penicillin in vitro, and in general the dose of penicillin given should be sufficient to maintain a concentration in the blood four or five times that required for inhibition of the infecting organism in vitro. While a dose of 400,000 to 1,000,000 units of penicillin daily will suffice in an average case, in the presence of a highly resistant strain or of relapses after treatment, doses up to 20,000,000 units daily may be required to effect a cure.

No rule can be laid down regarding the length of time treatment must be continued, for it varies with the conditions encountered in each patient. It is seldom wise to discontinue treatment in less than three weeks. Hunter [13] advised that treatment be stopped at the end of two to three weeks. A blood culture is then made; if this is negative, treatment is not resumed. He found that even though such a patient continues to have fever, leukocytosis, an increased sedimentation rate and embolic phenomena, it frequently turns out that a cure results without further treatment with penicillin. Such an interruption to test the question of a cure may shorten a laborious and uncomfortable treatment that otherwise might have been prolonged unnecessarily.

It is well recognized that a patient who has valvular heart disease can acquire subacute bacterial endocarditis after the extraction of a tooth and possibly after tonsillectomy. Such patients should always be protected by prophylactic treatment with penicillin. The administration of 100,000 units of penicillin every three hours for a day preceding and two days following such surgical procedures should suffice as a prophylactic measure.

ANTICOAGULANT THERAPY

Thromboembolism is a common and serious complication among patients suffering from heart failure or from acute coronary occlusion. Nay and I [14] studied the condition of 100 patients during their immediate convalescence from acute myocardial infarction. Thrombotic or embolic complications were observed in 37 cases. In 4 cases such complications were the cause of death, and in 8 they contributed importantly to death. These complicating episodes included a second myocardial infarction (15 cases), pulmonary embolism (14 cases) and cerebrovascular accidents (8 cases).

Preliminary experience [15] indicates that the routine administration of "dicumarol" to patients who have had an acute myocardial infarction greatly diminishes the incidence of thromboembolic episodes and promises to reduce materially the mortality rate of this condition.

The frequency with which embolism and pulmonary infarction complicate the treatment of heart failure is too well known to deserve comment. Since it is conceded generally that these emboli arise from thrombi in the veins of the legs, one group of investigators advocates ligation of the femoral or iliac veins if nonfatal pulmonary embolism has occurred. My colleagues and I have felt that we secured equally satisfactory results by treating these patients with "dicumarol." We feel that the bilateral ligation of large veins in the lower extremities is not wholly innocuous in its ultimate effects.

Pulmonary embolism occurring in medical and surgical cases ordinarily is not primarily a cardiac problem. Nevertheless, the ultimate survival of a patient who has had an attack of pulmonary embolism depends on the capacity of the heart to withstand the circulatory dis-

11. Grollman, A.: Sodium Restriction as a Dietary Measure in Hypertension, J. Am. Dietet. A. **22**: 864-866 (Oct.) 1946.
12. Grollman, A.; Harrison, T. R.; Mason, M. F.; Baxter, J.; Crampton, J., and Reichsman, F.: Sodium Restriction in the Diet for Hypertension, J. A. M. A. **129**: 533-537 (Oct. 20) 1945.
13. Hunter, T. H.: Treatment of Subacute Bacterial Endocarditis, Mod. Conc. Cardiovasc. Dis., August 1946, vol. 15.
14. Nay, R. M., and Barnes, A. R.: Incidence of Embolic or Thrombotic Processes During the Immediate Convalescence from Acute Myocardial Infarction, Am. Heart J. **30**: 65-76 (July) 1945.
15. Peters, H. R.; Guyther, J. R., and Brambel, C. E.: Dicumarol in Acute Coronary Thrombosis, J. A. M. A. **130**: 398-403 (Feb. 16) 1946. Nichol, E. S., and Page, S. W., Jr.: Dicumarol Therapy in Acute Coronary Thrombosis: Results in Fifty Attacks, with Review of Data on Embolic Complications and Immediate Mortality in Myocardial Infarction, J. Florida M. A. **32**: 365-370 (Jan.) 1946. Wright, I. S.: Experiences with Dicumarol (3,3'Methylene-bis-[4-Hydroxycoumarin]) in the Treatment of Coronary Thrombosis with Myocardial Infarction: Preliminary Report, Am. Heart. J. **32**: 20-31 (July) 1946.

turbances associated with this event. If a patient has an attack of pulmonary embolism after surgical treatment and survives for a few hours, he has a 44 per cent chance of having a subsequent thromboembolic episode and an 18 per cent chance of having a subsequent fatal embolism.[16] If treatment with heparin and "dicumarol" is started immediately after the episode and is administered properly, it has been shown that subsequent thromboembolic episodes can be prevented almost entirely.[17] If a patient gives a history of previous thrombophlebitis or pulmonary embolism, it is feasible to preclude almost all such occurrences after surgical treatment by starting "dicumarol" therapy on the third day after operation.

A successful dosage for "dicumarol," as employed at the Mayo Clinic, is as follows: The dose for the first day is 300 mg. On each subsequent day when the prothrombin is greater than 20 per cent of normal prothrombin, 200 mg. of "dicumarol" is given. On days when the prothrombin is less than 20 per cent of normal, no "dicumarol" is given. If the prothrombin drops below 10 per cent of normal during the first few days of treatment and remains there for two days, 20 to 30 mg. of menadione bisulfite is given intravenously, and thereafter only 100 mg. of "dicumarol" is given to that patient on those days on which the prothrombin is greater than 20 per cent of normal.[16]

"Dicumarol" cannot be administered safely unless its dosage is controlled by daily determination of the prothrombin time expressed in percentage of normal concentration of prothrombin. If serious bleeding occurs during the administration of "dicumarol," a transfusion of fresh citrated blood should be given. At the same time, 60 mg. of menadione bisulfite should be given intravenously and this dose should be repeated once or twice daily until bleeding ceases.

"Dicumarol" is contraindicated in the presence of purpura, subacute bacterial endocarditis, renal and hepatic insufficiency or for patients who recently have had an operation on the brain and spinal cord. It should not be administered in the presence of ulcerative lesions, such as ulcerative colitis.

THE SURGICAL TREATMENT OF HEART DISEASE

Patent Ductus Arteriosus.—Patent ductus arteriosus is characterized by an absence of cyanosis, a continuous murmur over the pulmonic area and roentgenographic evidence of enlargement of the pulmonary conus. The presence of a distolic murmur over the pulmonic area is almost essential if the diagnosis is to be established by ordinary clinical methods. If any doubt obtains about the diastolic murmur, its presence or its absence may be established if a phonocardiogram can be obtained. A thrill is present over the point of greatest intensity of the murmur in 75 to 80 per cent of the cases. The pulse pressure is increased above the normal of 30 to 45 mm. of mercury. Since both right and left ventricles are subject to strain and since hypertrophy of both is common, the electrocardiogram reveals no axis deviation or only slight deviation. Pronounced right axis deviation points to some other source of predominant right ventricular hypertrophy.

16. Barker, N. W.: Anticoagulant Therapy, Mod. Conc. Cardiovasc. Dis., November 1946, vol. 15.
17. Allen, E. V.: The Clinical Use of Anticoagulants: Report of Treatment with Dicumarol in 1,686 Postoperative Cases, J. A. M. A. **134:** 323-329 (May 24) 1947.

The indications for surgical closure of patent ductus arteriosus are (1) stunted growth, (2) an enlarging heart or symptoms of increasing dyspnea or both and (3) the presence of subacute bacterial endocarditis. Shapiro[18] urged that patients who have infected ducts should undergo early operation without waiting for a possible cure of the infection by penicillin.

Opinions differ concerning surgical intervention in cases in which the diastolic pressure is normal or only slightly reduced, in which there is little or no cardiac hypertrophy and in which there are no peripheral signs of edema. However, Keys and Shapiro[19] have estimated that the life expectancy of males is reduced by about twenty-three years and that of females by about twenty-eight years if a patent ductus arteriosus remains untreated. Since the mortality rate for surgical closure of patent ductus arteriosus is 5 per cent or less, Shapiro[18] is of the opinion that all children should undergo this operation as soon as the diagnosis is established regardless of apparent disability or signs of disruption of the cardiac function.

Whenever possible, section of the patent ductus arteriosus rather than ligation is the most effective as well as the most practical procedure.

Coarctation of the Aorta.—The prognosis of the adult type of coarctation of the aorta has been studied by Reifenstein, Levine and Gross.[20] They found one group of cases in which the patients had attained elderly life, had only minor complaints and had had a reasonably satisfactory life. The patients in the second group succumbed to a superimposed subacute bacterial infection. In a third group, sudden death occurred from rupture of the aorta. In a fourth group, death occurred from cardiac decompensation or from intracranial hemorrhage. In general, they found that although some persons enjoy a long life, the prognosis usually is poor for survival beyond the ages of 25 to 30 years.

Gross[21] in this country and Crafoord[22] in Sweden have demonstrated the feasibility of the surgical treatment of coarctation of the aorta. Gross has operated on 14 patients for this condition, with 2 deaths. In 1 a satisfactory anastomosis could not be obtained, but the patient survived the operation without any significant change in his hypertensive state. In the remaining 11 cases the results of the operation were satisfactory: Normal pulsations and pressures were restored in the arteries of the legs, and hypertension in the upper part of the body was relieved completely.

Gross considered that "the optimal ages for performance of this operation lie between 6 and 20 years." Beyond the age of 25 years arteriosclerosis "makes the aorta a poor vessel for manipulation and suture." It is obvious that the early identification of coarctation of the aorta offers the patient the best chance for surgical treatment, and hence for survival.

Congenital Pulmonic Stenosis.—In May 1945, Blalock and Taussig,[23] in an epochal report, described the first successful operation for the relief of pulmonary

18. Shapiro, M. J.: Recent Advances in Surgical Treatment of Patent Ductus Arteriosus, Mod. Conc. Cardiovasc. Dis., January 1947, vol. 16.
19. Keys, A., and Shapiro, M. J.: Patency of the Ductus Arteriosus in Adults, Am. Heart J. **25:** 158-186 (Feb.) 1943.
20. Reifenstein, G. H.; Levine, S. A., and Gross, R. E.: Coarctation of Aorta: A Review of One Hundred Four Autopsied Cases of the 'Adult' Type, Two Years of Age or Older, Am. Heart J., to be published.
21. Gross, R. E.: Technical Considerations in Surgical Therapy for Coarctation of the Aorta, Surgery **20:** 1-8 (July) 1946.
22. Crafoord, C., and Nylin, G.: Congenital Coarctation of Aorta and Its Surgical Treatment, J. Thoracic Surg. **14:** 347-361 (Oct.) 1945.
23. Blalock, A., and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. **128:** 189-202 (May 19) 1945.

stenosis. They stated that the operation was indicated in cases of congenital cardiac lesions producing cyanosis when there was clinical and roentgenographic evidence of an inadequate flow of blood through the lungs. The evidence for this rests on "the absence of visible pulsations in the lung fields as observed under the fluoroscope and roentgenographic evidence that the pulmonary artery is small in size." [23] When a patient is of sufficient age so that catheterization of the heart by the venous route is feasible, this procedure may yield information which not only confirms the diagnosis, but also is a means of determining the volume of the pulmonary blood flow. In any event, if the diagnosis is doubtful in the case of a child who has decided cyanosis and if the prognosis for the patient is considered hopeless, Blalock and Taussig have considered that exploration is justified. When the pulmonary artery is exposed, the pressure in the artery can be measured by a water manometer attached to a needle which is inserted into the pulmonary artery. These observers considered operation inadvisable if the pressure in the pulmonary artery is more than 300 mm. of water.

Blalock and Taussig have reported that the operation is beneficial in (1) tetralogy of Fallot, (2) pulmonary atresia with or without dextroposition of the aorta and with or without defective development of the right ventricle, (3) truncus arteriosus with bronchial arteries and (4) a single ventricle with a rudimentary outlet chamber with which the pulmonary artery is diminutive in size.

Blalock [24] has reported operation on 110 patients for congenital pulmonic stenosis with an over-all mortality rate of 23 per cent. In some of these cases the operation consisted of exploration and anastomosis was not performed.

The operation results in a decrease of cyanosis, and clubbing of the fingers and toes diminishes after a period. The tolerance of the children to exercise is increased greatly after operation, and some then can engage in fairly strenuous exercise.

ABSTRACT OF DISCUSSION

TREATMENT OF HYPERTENSION

QUESTION: Is the surgical treatment of hypertension the most satisfactory way of treating this disease?

ANSWER: Not necessarily. The selection of the method of treating a patient with hypertension must rest on the careful analysis of the individual case. This study must include an attempt to discover the cause of hypertension. If coarctation of the aorta is discovered, surgical treatment of that condition is in order. If a unilateral functionless kidney is found, its removal may relieve the hypertension. If the hypertension is found to be associated with chronic nephritis, sympathectomy is unwarranted. Sympathectomy for hypertension beyond the age of 55 years is of limited or questionable value. Hypertension in young patients should be followed for some time to determine whether it is periodic in occurrence or shows a tendency to be progressive in its severity. Sympathectomy is probably indicated in the latter case but is of doubtful value in the former. The indications for sympathectomy are clearest in patients less than 50 years of age who have severe hypertension and in whom cerebral vascular accidents have not occurred, who have not had heart failure in association with pronounced cardiac hypertrophy and in whom serious renal damage has not occurred. An additional indication for operation in these cases is the occurrence of severe headaches.

24. Blalock, A.: The Surgical Treatment of Congenital Pulmonic Stenosis, Ann. Surg. **124**: 879-887 (Nov.) 1946.

GLYCOSIDES OF DIGITALIS

QUESTION: Are the purified glycosides of digitalis more useful than the powdered leaf in the treatment of heart disease?

ANSWER: One of the purified glycosides of digitalis, digitoxin, has two chief advantages. The first advantage is that a full digitalizing dose of this preparation may be given by mouth at one time with minimal prospects of producing nausea and vomiting, and the second is that by virtue of the fact that digitoxin is absorbed 100 per cent in the gastrointestinal tract, it is easier to predict the amount of the drug that must be given by mouth to produce a full effect of digitalis. However, it must be recognized that there is considerable individual variation in the amount of the drug required to produce the desired effect. The purified glycoside lanatoside C has the disadvantage that only about a tenth of the orally administered dose is absorbed in the gastrointestinal tract. Nausea and vomiting are somewhat less commonly observed in patients adequately treated with purified glycosides of digitalis than when a similar effect of digitalis is obtained by the use of a preparation of the powdered leaf.

LOW SODIUM DIET

QUESTION (Dr. Maurice D. Krauss, Brooklyn): Is there any value in a low sodium diet in compensated valvular disease?

ANSWER: A low sodium diet is indicated in a patient with compensated valvular disease of the heart who has suffered from previous cardiac decompensation. If the patient has had no such episode of cardiac decompensation, one is not warranted in subjecting him to the inconvenience of a low sodium diet.

CORONARY THROMBOSIS

QUESTION (Dr. O. P. J. Falk, St. Louis): Do you feel that heparin should be added to "dicumarol" therapy in coronary thrombosis?

ANSWER: No. If a dose of 300 mg. of "dicumarol" is given immediately after acute coronary thrombosis, an adequate effect on the coagulability of the blood will be obtained in forty-eight to seventy-two hours. Thromboembolic episodes are extremely unlikely to occur in the first two or three days after acute coronary occlusion.

DOSAGE OF HEPARIN AND "DICUMAROL"

QUESTION (Dr. H. S. Connanmacher, Newark, N. J.): What doses and what frequency do you use with heparin and "dicumarol"?

ANSWER: Heparin is given intravenously by two methods. 1. It may be given by a continuous drip method starting at 25 drops per minute and varying the rate of injection so that the coagulation time of venous blood is kept between fifteen and twenty-five minutes. The intravenous solution is made by adding 100 to 200 mg. of heparin to 1,000 cc. of a diluent, either a 0.9 per cent solution of sodium chloride or a 5 per cent solution of dextrose. 2. A concentrated solution of heparin of either 5 cc. (50 mg. of heparin) given every four hours or 10 cc. (100 mg. of heparin) given every six hours may be administered intravenously. With this latter method the coagulation time is not followed, and despite the fact that the coagulation time returns to normal between injections, the method seems to be effective. Heparin may be given subcutaneously or intravenously in the Pitkin menstruum every two or three days (Loewe, L., and Rosenblatt, P.: A New Practical Method for Subcutaneous Administration of Heparin; Preliminary Report. *Am. J. M. Sc.* **208**:54-63 [July] 1944. Barker employs the following dosage schedule for "dicumarol" at the Mayo Clinic: The entire amount for one day is given in a single dose. The first dose is 300 mg. On each subsequent day when the prothrombin is greater than 20 per cent of normal prothrombin, 200 mg. of "dicumarol" is given. On days when the prothrombin is less than 20 per cent of normal, no "dicumarol" is given. If the prothrombin drops below 10 per cent of normal during the first few days, 20 to 30 mg. of menadione bisulfite is given intravenously, and thereafter only 100 mg. of "dicumarol" is given to that patient on those days on which the prothrombin is greater than 20 per cent of normal. With this schedule, prothrombin deficiency has been maintained for as long as six months without untoward or toxic effect on

the patient and with return of prothrombin to normal within a few days after administration of "dicumarol" finally was discontinued.

WILSON'S UNIPOLAR LEAD

QUESTION (Dr. Peter Pileggi, Bridgeport, Conn.): Please say a few words on the value of Wilson's unipolar lead, especially in the diagnosis of cases of acute coronary thrombosis when other leads are negative?

ANSWER: This question does not relate to treatment and cannot be discussed in the limited scope afforded for answers to these questions.

TREATMENT OF RHEUMATIC HEART DISEASE

QUESTION: Are there effective methods of treating and preventing rheumatic heart disease?

ANSWER: Yes, with certain limitations. 1. In treatment of an acute attack of rheumatic fever salicylates should be administered in large doses by mouth to lower the fever, control pain and reduce the sedimentation rate, but this does not constitute a cure of the disease. The patient should be kept at rest in bed until evidences of activity of the rheumatic fever process have disappeared. Beyond this, activity may be gradually resumed, but it is important to isolate the patient for several months from contacts which might allow him to acquire an acute infection of the respiratory tract. 2. In a child that has had one or more attacks of rheumatic fever, the daily administration of sulfadiazine, except possibly during the summer months, seems definitely to diminish the likelihood of his having a recurrence of rheumatic fever. Improvement of the environment, including adequate housing, clothing and food, and the avoidance of excessive fatigue in the succeeding preadult years add greatly to the protection that can be afforded against recurrent attacks of rheumatic fever. Children who have had rheumatic fever are better protected from recurrences by residence in a warm climate. Their hazard is increased by residence in children's homes or in large families where the chance of acquiring acute infections of the respiratory tract is greatly increased.

USE OF HEPARIN

QUESTION: Has the use of heparin in subacute bacterial endocarditis any value?

ANSWER: It is the consensus that it has no use in this condition. In my personal experience, the use of heparin in the treatment of subacute bacterial endocarditis has led to serious complications.

USE OF THIOURACIL

QUESTION (Dr. Benjamin Miller, Baltimore): Please discuss the use of isopropyl thiouracil in heart disease; that is, cases that are not directly thyrogenic in etiology.

ANSWER: The usefulness of isopropyl thiouracil in the treatment of heart disease is predicated on its function of reducing the basal metabolic rate. The care that must be exercised to be certain that neutropenia does not result, and the untoward general effects produced if very low basal rates are reached, greatly reduce its usefulness for practical purposes. The result of its use in the treatment of heart disease to date is not sufficiently demonstrated to warrant its general use for this purpose.

MERCURIAL DIURETICS

QUESTION: (Dr. H. W. Stevens, Middleboro, Mass.): What benefits can be effected by mercurial diuretics that are not possible by careful control of sodium intake and other control of diet and activity?

ANSWER: Most cases of heart failure are controlled by a low sodium intake, the judicious use of digitalis preparations and control of the patient's activity. However, practical experience has shown that in spite of these measures, edema in some cases can be controlled only by the periodic administration of mercurial diuretics.

SODIUM PENICILLIN

QUESTION (Dr. Edward R. Barber, Lancaster, S. C.): Is the sodium in sodium penicillin present in sufficient amounts to cause harm in a patient with congestive heart failure and to warrant the use of another type of penicillin?

ANSWER: The amount of sodium in sodium penicillin is so small as scarcely to be a factor in the production of edema when administered to a patient with congestive heart failure. If there were any question, the penicillin could be given as calcium penicillin, which is the form in which I administer most of the penicillin given under my supervision.

USE OF POTASSIUM CHLORIDE

QUESTION (Dr. Glen Pincock, Washington, D. C.): In cardiac decompensation is the substitution of potassium chloride as "salt" in place of sodium chloride advisable?

ANSWER: In cardiac decompensation potassium chloride may be substituted as "salt" for sodium chloride if the patient finds it renders his food more palatable.

USE OF THIOCYANATES

QUESTION: How safe are thiocyanates for use by general practitioners?

ANSWER: Thiocyanates can be used most safely only if their dosage is controlled by periodic determinations of the levels of the cyanates in the blood. If a patient has been followed over a sufficient period of time with determination of levels of the cyanates in the blood and if a safe dosage level has been established, he usually may continue that dose under the direction of his home physician. Even then, the patient should be instructed to report to his physician if a cutaneous rash or gastrointestinal symptoms appear. Most patients will tolerate a dose of 6 grains (0.4 Gm.) of potassium thiocyanate daily without the risk of untoward symptoms, but often that dose does not produce blood levels sufficiently high to be very useful in the treatment of hypertension. Physicians should also be aware that the thiocyanates may produce myxedema and should be alert for signs of its development.

ANTICOAGULANTS

QUESTION (Dr. Paul A. Sica, Pittsburgh: Are you routinely using anticoagulants in all your cases of acute myocardial infarction?

ANSWER: Yes.

QUESTION (Dr. E. P. Bray, Richmond, Va.): In acute myocardial infarction when and how would one start anticoagulant therapy?

ANSWER: See answers to the fourth and fifth questions.

HYPERTENSIVE ENCEPHALOPATHY

QUESTION: Please discuss the use of hypertonic sugar solution and magnesium sulfate in hypertensive encephalopathy. Please discuss the changes in blood lipids which are responsible for the appearance of lipemia retinalis and xanthoma diabeticorum.

ANSWER: This is too much to attempt to answer in the scope allowed for answers to such questions.

SYPHILITIC ANEURYSM

QUESTION (Dr. R. Weyher, Detroit): Is penicillin therapy justified in an early thoracic syphilitic aneurysm with mild cardiac failure?

ANSWER: In general the answer is no. There are reports of deaths due to Herxheimer reactions in patients treated with large doses of penicillin for syphilis of the aorta. If penicillin is used in such a situation, great care should be taken and small doses of penicillin employed over a long period of time. One could not expect improvement in the aneurysm. The cardiac failure would have to be treated by the usual measures employed in treating such a condition if it were of nonsyphilitic origin.

IDIOSYNCRASY TO QUINIDINE

QUESTION (Dr. A. Alexander Bernstein, Scranton, Pa.): When patients show an idiosyncrasy to quinidine, in auricular fibrillation, what do you use?

ANSWER: I have little to offer anybody who is permanently sensitive to quinidine, but I would remind the man who asked this question that by stopping quinidine it may be possible to resume its use later and have the patient take it successfully.

RECENT ADVANCES IN TREATMENT OF CANCER

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The pattern of recent advances in the treatment of cancer differs somewhat from that of the past. It represents, perhaps, an indication of a new trend, long foreseen, toward more radical surgery on the one hand and toward new biochemical approaches on the other. This denotes a strengthening of the position of surgery as a curative agent, coincidentally with an intensified search for new means of palliation and control.

The procedure devised by Mohs,[1] entitled "Chemosurgical Treatment of Cancer," has recently been the subject of a review of five year end results of its application to neoplasms of the ear. The method is beyond question an interesting one and deserving of careful consideration. Of 19 patients with squamous cell carcinoma treated, 9 are well after five years. It is unfortunate that no figure is given for the five year salvage in cases of disease recurrent after efforts at therapy by other means. It is stated that 53 per cent of patients with recurrent disease were successfully treated, but the duration of the success is not specified. The same objection can be raised to the figures reported for the treatment of basal cell carcinoma. Here 81 per cent of five year cures are reported, but no duration for the 76 per cent cures of recurrent disease. The cure rates for skin cancer adequately treated by conventional surgical or radiologic means are, of course, exceedingly high also.

CANCER OF THE UPPER RESPIRATORY TRACT

Nowhere is the drift toward more radical surgery seen more clearly than in the treatment of neoplasms of the oral cavity and the upper respiratory tract. Unfortunately cancer of the mouth and associated structures varies greatly in prognosis according to site. As a result statistical proof of the value of the extensive surgery now practiced is not yet at hand. Sufficient evidence is available, however, to suggest that much oral disease, now frequently classified as suitable for only palliative care, is actually susceptible of cure if bold measures are undertaken by competent operators.

The question of the most effective treatment of laryngeal cancer is still debated in some circles. A review of the results of radiation therapy of cancer of the larynx has recently been published by Lenz.[2] Of 110 patients studied, 30 are reported to be free of disease for periods of over five years. He recommends roentgen therapy for all cancers of the vocal cord except when disease has extended subglottally or into the arytenoid cartilage. This conclusion is based on 8 survivals of 10 patients treated. The report of Cutler[3] suggests that a five year cure rate of 60 per cent, as high as the one seen after surgery, can be obtained by the use of roentgen rays alone in patients who would normally have been subjected to laryngectomy. The experience on which this opinion is based, however, seems to be limited to a total of 10 patients, as far as can be concluded from the published data. In a more recent report[4] 18 five year cures, or 42 per cent of 47 patients treated, are reported. There can be no doubt whatever that certain patients with laryngeal disease are and should be cured by roentgen irradiation. The loss of voice and the hazard associated with the surgical removal of the larynx have been in the past serious deterrents to operative intervention in general. Modern technics for the development of the esophageal voice and the ability of Martin and his associates[5] to perform one hundred and ninety-three total laryngectomies for cancer with only 3 operative fatalities (1½ per cent), including a series of 102 consecutive cases without any postoperative death, and a cure rate of about 60 per cent in 44 cases in which operation had been performed more than five years previously, have altered the situation. It is hard to conceive of diagnostic criteria and acumen so accurate as to make possible a uniformly reliable decision as to whether a given example of laryngeal cancer is capable of being cured by roentgen irradiation. On the basis of the facts now available, surgery undoubtedly sacrifices some larynxes which could have been saved by radiation therapy. Surgical intervention probably saves 50 per cent more lives, however, a significant number, and many prefer their lives to their larynxes.

CANCER OF THE BREAST

The treatment of cancer of the breast remains surgical as far as cure is concerned. The procedures employed are so standardized as to be hardly worth comment. One set of facts deserves attention, however. In one clinic amputating, without skin graft, more than five hundred breasts annually for cancer, the five year cure rate for all patients found to have involvement of axillary lymph nodes is 46 per cent, the postoperative mortality 0.2 per cent and the incidence of local skin recurrence not over 19 per cent. These figures indicate that the exceedingly radical procedure frequently advocated for all amputations of the breast for cancer is not always required. They fail to support the feeling of some that no true, wholly autonomous cancer is ever cured.

The palliative care of patients with metastatic disease of the breast provides an interesting and important development. Here hormone therapy clearly is irregularly and transiently effective. The early reports of Fels[6] and of Loeser[7] have been supported by the observations published recently by Adair and Herrmann.[8] The administration of testosterone propionate in doses adequate to cause masculinization brings about irregularly demonstrable calcification of previously decalcified areas of mammary cancer metastatic to bone. This

Read in a Panel Discussion on Recent Advances in Treatment before the joint meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 13, 1947.

1. Mohs, F. E.: Chemosurgical Treatment of Cancer of the Ear: A Microscopically Controlled Method of Excision, Surgery **21**: 605, 1947.
2. Lenz, M.: Cancer of the Larynx, J. A. M. A. **134**: 117 (May 10) 1947.
3. Cutler, M., in Report of the Chicago Tumor Institute, April 1, 1938 to March 31, 1945.
4. Cutler, M.: Cancer of Larynx: Five-Year Results of Concentration Radiotherapy, Arch. Otolaryng. **43**: 300 (April) 1946.
5. Martin, H.: Cancer of the Larynx, in Nelson's Loose Leaf Surgery, New York, Thos. Nelson & Sons, 1947.
6. Fels, E. J.: Treatment of Breast Cancer with Testosterone Propionate, J. Clin. Endocrinol. **4**: 121, 1944.
7. Loeser, A. A.: Mammary Carcinoma Response to Implantation of Male Hormone and Progesterone, Lancet **2**: 698, 1941.
8. Adair, F. E., and Herrmann, J. B.: The Use of Testosterone Propionate in the Treatment of Advanced Carcinoma of the Breast, Ann. Surg. **123**: 1023, 1946.

seems to occur in over 15 per cent of the patients treated and to be of variable duration. Subjective improvement, indicated by gain in weight and relief of pain, can be striking. Certain patients are encountered, however, as first described by Farrow and Woodard,[9] whose blood calcium levels are somewhat elevated before treatment is begun, in whom profound and possibly dangerous hypercalcemia follows administration of testosterone. In these persons pain may be relieved coincidentally with a rapid and extensive spread of the metastatic neoplasm.

The use of estrogenically active substances, particularly diethylstilbestrol, in the treatment of metastatic cancer of the breast was initially described in England.[10] It has been explored further in this country, particularly by Nathanson.[11] The beneficial effects are seen principally when soft tissues are involved. This contrasts sharply with the results of testosterone therapy, which are almost entirely seen in metastases to bone. The incidence of improvement of soft tissue lesions is about the same (15 per cent) as the improvement of osseous lesions after testosterone therapy. Similar complications may occur, and improvement is equally transient.

The review by Halberstaedter[12] of the effects of oophorectomy on patients with metastatic disease of the breast deserves to be consulted. It is an odd fact that this procedure, so often reestablished as useful, continues to need defense.

ABDOMINAL CANCER

The radical surgery of abdominal cancer has been the subject of a major contribution by Brunschwig.[13] This surgeon reports the results of one hundred very extensive operative procedures. The patients had cancer which had extended locally to invade organs other than the one primarily involved. Fifty per cent of the patients were early fatalities or received no palliative benefit; 37 per cent returned to their usual occupations only for periods of from weeks to months, and 13 per cent have been free of disease for two to ten years. The policy adopted by Brunschwig of attempting, at least, the removal of locally invasive disease, inoperable by ordinary standards, has been criticized on the score of practically every criterion of culpability. The logic in these criticisms is hard to ascertain. The cure rate obtained, 13 per cent, is as high as that for all patients treated for rectal cancer in the state of Connecticut,[14] higher than the cure rates for neoplastic disease of lung, stomach, bone and bladder. There can, indeed, be no logical argument against the use of heroic measures to save life. The 13 patients salvaged of the 100 treated certainly represent pure gain. They are willing, I feel sure, to pay tribute to the determination, vision and technical ability of the surgeon.

CANCER OF THE THYROID GLAND

The treatment of cancer of the thyroid gland by radioactive iodine is a possibility which has been hailed with great enthusiasm by those who deal with the manufacture of atomic bombs, because of the humane application of the by-products. The primary observations of Hamilton[15] and of Frantz[16] that radioactive iodine was stored in several of a large number of metastatic nodules of a primary thyroid adenocarcinoma has led to further studies. Seidlin, Marinelli and Oshry[17] have reported on the treatment with radioactive iodine of an extraordinary patient. This person had hyperthyroidism from functioning metastases of thyroid adenocarcinoma. The normal thyroid had been wholly removed and there was no uptake of radioactive iodine by the tissue of the neck. Thyroxin iodine was demonstrated in the metastases and thiouracil produced a complete remission of the hyperthyroidism. This recurred when the drug was withdrawn. Therapy with I^{131} has controlled not only the hyperthyroidism but also the cancer for over four years.

Particularly pertinent to the problem of treatment of thyroid cancer is the study of Marinelli, Foote, Hill and Hocker.[18] An effort was made to correlate the pick-up of radioactive iodine with the histologic type of thyroid neoplasms. Detectable deposition of radioactive iodine was found in only about 15 per cent of thyroid cancers. As might have been expected, deposition of iodine was greatest in metastasizing struma and least in the more anaplastic types of solid carcinoma. It is to be hoped that some procedure can be devised for increasing the uptake of iodine by the less differentiated tumors of the thyroid. If this is not done, therapeutic successes are likely to be few.

CANCER OF THE BLADDER

The recent communications of Jewett[19] and of Marshall[20] concerning cancer of the bladder merit particular attention. Jewett in a careful study proved that in about 25 per cent of patients whose cancer of the bladder has infiltrated the muscular wall there is no extension into adjacent structures. Marshall reported a postoperative mortality for ureteral transplantation and total cystectomy of approximately 10 per cent and a five year cure rate for cancer of the bladder treated by radiation of 6 per cent. From these facts it appears likely that the more extensive use of total cystectomy in the future should result in a significant improvement in rate of cure, since the disease of many patients in the group reported by Jewett should be susceptible to control by surgery.

THE NITROGEN MUSTARDS

The most noteworthy advance in the treatment of neoplastic disease during 1946 has been in the use of the nitrogen mustards. From the days of World

9. Farrow, J. H., and Woodard, H. Q.: The Influence of Androgenic and Estrogenic Substances on the Serum Calcium in Cases of Skeletal Metastases from Mammary Cancer, J. A. M. A. **118**: 339 (Jan. 31) 1942.

10. Haddow, A.; Watkinson, J. M., and Paterson, E.: Influence of Synthetic Oestrogens upon Advanced Malignant Disease, Brit. M. J. **2**: 393, 1944.

11. Nathanson, I. T.: The Effect of Stilbestrol on Advanced Cancer of the Breast, Cancer Research **6**: 484, 1946.

12. Halberstaedter, L., and Hochman, A.: The Artificial Menopause and Cancer of the Breast, J. A. M. A. **131**: 810 (July 6) 1946.

13. Brunschwig, A.: Radical Surgery in Advanced Abdominal Cancer, Chicago, University of Chicago Press, 1947.

14. Oppenheimer, E.: Carcinoma of the Rectum in Connecticut, New England J. Med., to be published.

15. Hamilton, J. G.; Soley, M. H., and Eichorn, K. B.: Deposition of Radioactive Iodine in Human Thyroid Tissue, Univ. of California Publ., Pharmacol. **1**: 339-368, 1940.

16. Frantz, V. K.; Ball, R. P.; Keston, A. S., and Palmer, W. W.: Thyroid Carcinoma with Metastases Studied with Radioactive Iodine, Ann. Surg. **119**: 668, 1944.

17. Seidlin S. M.; Marinelli, L. D., and Oshry, E.: Radioactive Iodine Therapy: Effect on Functioning Metastases of Adenocarcinoma of the Thyroid, J. A. M. A. **132**: 838 (Dec. 7) 1946.

18. Marinelli, L. D.; Foote, F. W.; Hill, R. F., and Hocker, A. F.: To be published.

19. Jewett, H. J.: Infiltrating Carcinoma of the Bladder: Application of Pathologic Observations to Clinical Diagnosis and Prognosis, J. A. M. A. **134**: 496-500 (June 7) 1947.

20. Marshall, V. F.: A Comparison of Radiation and Surgery for Cancer of the Bladder, J. A. M. A. **134**: 501-507 (June 7) 1947.

War I it has been known that mustard gas injures hemopoietic tissue. Studies of chemical warfare agents jointly by Army and Office of Scientific Research and Development contractors confirmed the fact and extended knowledge of the details. Gilman,[21] while a contractor working under military secrecy, was the first to apply the mass of new pharmacologic knowledge to the treatment of a patient with lymphosarcoma. Later Jacobson,[22] also on a war research contract, extended the observation and found particularly good effects in Hodgkin's disease. In 1944 the most promising nitrogen mustard, commonly termed HN_2, was made available by the Office of Scientific Research and Development to the National Research Council for distribution to three representative institutions for the treatment of patients. A summary of the results obtained appeared in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.[23] During the past year it has been available on request to institutions qualified under the rulings of the Food and Drug Administration. Over five thousand treatment units have been distributed to one hundred and twenty-six institutions and over one thousand one hundred clinical reports have been received. Of these about 60 per cent provide data suitable for analysis. The study has been supervised by a representative of the Committee on Growth of the National Research Council, Dr. David Karnofsky. The results can be summarized as follows, though exceedingly incomplete:

1. Hodgkin's disease. About 70 per cent of the patients with Hodgkin's disease show objective improvement and about 90 per cent subjective response. Remissions last about one month in most instances, but may rarely endure as long as six months. Responses can be obtained to subsequent courses of treatment.

2. Myeloid leukemia. Full remissions can be induced in early and moderately advanced stages of myeloid leukemia. These remissions are of the type which results from roentgen irradiation but tend to be of shorter duration.

3. Lymphosarcoma and lymphatic leukemia. Improvement in cases of lymphosarcoma and lymphatic leukemia can be obtained but tends to be of limited degree and transient. Severe toxic reactions of the hemopoietic system are common and the use of the drug is not recommended.

4. Acute leukemia seems not to be influenced favorably in its course.

5. Cancer of the gastrointestinal tract, oral cavity, breast and genitourinary systems is not inhibited.

6. Cancer of the lung can be caused to regress temporarily in about 50 per cent of the instances. The effects are transient and incomplete.

7. Melanoma and tumors of the central nervous system may possibly respond to some extent. More information is needed.

The advances described and recently reported are not events of 1946 alone. They represent the accumulated force of the experience of a considerable period. They, coupled with new mechanisms for early diagnosis and mass examination, have already lessened the age-adjusted death rate from cancer. The intense public resolution to be rid of the threat of this grave disorder bids fair to provide rapid progress in the future.

21. Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the B-Chloroethyl Amines and Sulfides, Science **103**: 409, 1946.
22. Jacobson, L. O.; Spurr, C. L.; Guzman Barron, E. S.; Smith, T.; Lushbaugh, C., and Dick, G. F.: Nitrogen Mustard Therapy, J. A. M. A. **132**: 263 (Oct. 5) 1946.
23. Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Disease, J. A. M. A. **131**: 656 (Jne 22) 1946.

ABSTRACT OF DISCUSSION

HODGKIN'S DISEASE

QUESTION (Dr. Robert D. Redston, New York): Has it been observed that cases of Hodgkin's disease progress more rapidly toward termination after treatment with nitrogen mustard and a remission of variable duration?

ANSWER: From the survey which has been made under the auspices of the National Research Council there is no reason to believe that Hodgkin's disease progresses more rapidly toward termination after nitrogen mustard therapy, followed by remission.

CANCER OF PROSTATE

QUESTION: What is the most effective chemical treatment of carcinoma of the prostate?

ANSWER: Adequate data are not at hand to answer this question. There is no doubt whatever that diethylstilbestrol or its derivatives have a distinct though temporary clinical effect. It is commonly supposed that the effect is due to the estrogenic potency of the chemical used.

ESTROGENS AND CANCER OF BREAST

QUESTION: Is there danger in producing cancer of the breast with the use of estrogenic substances?

ANSWER: I know of no danger of producing cancer of the breast by the administration of estrogenic substances. A very few reports are available of patients in whom cancer of the breast developed after intensive therapy with estrogens. In view of the extensive use of estrogens in treatment, and the comparatively common nature of cancer of the breast, few workers in the field believe there is any connection between the administration of hormone and neoplastic change. The doses of estrogenic hormone used to induce mammary cancer in susceptible strains of animals are far larger than those used in human therapy.

TREATMENT OF CANCER

QUESTION: Are there any new chemicals effective in the treatment of cancer?

ANSWER: I know of no new chemicals which have been proved to be effective in the treatment of cancer in man.

GASTRIC CANCER

QUESTION (Dr. F. G. Kojis, New York): What is the effect of estrogens on gastric carcinoma?

ANSWER: No effect has been shown to be exerted by estrogens on the course of gastric carcinoma.

USE OF TESTOSTERONE IN CANCER OF THE BREAST

QUESTION (Dr. Clarence Bernstein, Orlando, Fla.): What is the average dosage of testosterone propionate in the treatment of metastases of breast cancer (in a patient of average weight), with pleural effusion? Is there any real danger of overdosage and what would be the clinical or physiologic effects?

ANSWER: The usual dose of testosterone propionate in the treatment of osseous metastasis from cancer of the breast is 25 mg. daily by intramuscular injections. The development of marked symptoms of masculinization is an indication for decreasing the dose. The compound should be used to its biologic effect. There is real danger of overdosage in certain rare patients; in these persons severe hypercalcemia may occur and be marked by all the usual symptoms of this disorder. Patients receiving testosterone propionate therapy should be checked at regular intervals for blood calcium levels.

SURGERY FOR ABDOMINAL CANCER

QUESTION (Dr. Wilfred Dorfman, Brooklyn): Please discuss in further detail the type of surgery used for abdominal cancer. What type of case can be helped?

ANSWER: For an answer to this question the recently published book by Dr. Alexander Brunschwig, entitled "Radical Surgery in Advanced Abdominal Cancer" (1947, Chicago, University of Chicago Press) should be consulted. Most of the patients who were helped by Dr. Brunschwig were those who had considerable local extension of the primary cancer without blood-borne metastases.

TREATMENT OF MULTIPLE MYELOMA

QUESTION (Dr. Nathan Schechter, Ottawa, Ontario, Canada): What is the best treatment of multiple myeloma?

ANSWER: The course of multiple myeloma untreated is so variable that firm conclusions as to the best method of therapy are difficult to formulate. The use of such compounds as "stilbamidine" (4,4'-diamidinostilbene) is still in the experimental phase.

HEMATOLOGY

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Important advances in hematology during the past year concern the use of folic acid in anemia and further trial of radioactive isotopes and other new chemicals in the treatment of leukemia and polycythemia. The therapeutic application of folic acid has reemphasized also the need for an accurate laboratory study and classification of the anemias before treatment is begun, since this drug is indicated only with macrocytosis.

FOLIC ACID

Synthetic folic acid (pteroylglutamic acid) is now available in unlimited quantities. It is of value only in a macrocytic anemia with a megaloblastic bone marrow. Important examples of such an anemia are (1) idiopathic pernicious anemia, when there is deficient formation of a specific erythrocyte-maturing factor (EMF); (2) macrocytic nutritional anemia in children due to a defect in supply or absorption, the macrocytic anemia of pregnancy due to increased need and the macrocytic anemia of adults dependent on a defective absorption of the specific substances resulting from a small bowel lesion such as obstruction or multiple anastomoses; (3) sprue, and (4) pellagra. There is no evidence that folic acid helps in a hypochromic anemia due to a deficiency of iron or in the normocytic anemias due to other causes such as infection, malignancy or increased hemolysis. Folic acid may well be the specific substance needed by the developing red cell to complete its development in the marrow before release into the blood stream. Growing red cells lacking this substance are larger than normal, so that macrocytosis is an indication of a need for the drug. The routine use of folic acid in every type of anemia is to be deplored.

Folic acid when given in sufficient amounts in a properly diagnosed and selected case will relieve the anemia and macrocytosis with a return of the blood to normal. The glossitis, diarrhea, weakness and anorexia often seen in such patients may be relieved entirely also. The drug is quickly absorbed and is effective by mouth. It seems the drug of choice in the treatment of the macrocytic anemia of sprue, pellagra, pregnancy and other nutritional disturbances. Probably the nutritional defect is the same in each instance; namely, a loss of supply or absorption of a specific substance which may be folic acid. All such conditions are responsive to the administration of a potent liver extract, so that folic acid is replacing an already satisfactory treatment largely because it may be given in any amount and by mouth rather than by hypodermic injection.

Should folic acid replace liver extract in the treatment of pernicious anemia? This is a complicated disease involving (1) the hemopoietic system, (2) the gastrointestinal tract and (3) the peripheral and central nervous systems. The disease is a primary defect in the gastric mucosa resulting in a defective formation of the specific erythrocyte-maturing factor (EMF) also deficient in the macrocytic anemias already discussed. The exact cause of the lesion in the nervous system has never been clear, although it seems evident that there is something lacking which is necessary for the normal nutrition of nerve tissue. It has not been known whether this is the same substance needed to form red cells, although it has been evident to all hematologists that the symptoms and signs referable to the nervous system were benefited and often relieved by adequate liver therapy. Perhaps experiences with folic acid have cleared up this question.

The macrocytic type of pernicious anemia is cured completely by the use of folic acid, probably because a specific deficiency is supplied. There is no evidence, however, that folic acid has any influence on the neurologic lesion of pernicious anemia. On the contrary, experience suggests that the lesions in nerve and spinal cord may develop rapidly even with folic acid therapy adequate to relieve the anemia. The neurologic lesion is the most disabling and serious phase of pernicious anemia. Once well developed it is difficult to help by treatment, so that any treatment which does not influence the neurologic lesion should not be used.

Folic acid should not be used for the routine treatment of pernicious anemia. Liver extract remains the treatment of choice for this disease. Properly carried out it is almost a perfect treatment for pernicious anemia. There is no evidence that the addition of folic acid to liver extract enhances its value in pernicious anemia. It only adds to the cost. In patients allergic to liver extract the best substitute is folic acid. Such a condition is rare, however, and can usually be handled by changing the brand of the liver extract used. In our large series colleagues and I have encountered no patient whom we could not treat with some liver extract.

Folic acid, while not satisfactory for the treatment of pernicious anemia, has helped in clarifying the mode of action of liver extract in the macrocytic anemias. Liver extract has been thought of in the past as actually supplying some missing substance necessary for the normal growth of red cells and for the nutrition of nerve tissue. Liver extract does contain a small amount of folic acid but not enough to explain its beneficial effect on blood formation. Recent work indicates that the liver extract activates substances needed by erythrocytes and nerve tissue through its general action on cellular

From the Cleveland Clinic.
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metabolism. It has been suggested that so far as the red cells are concerned the action of liver extract is to free folic acid (pteroylglutamic acid) from its inactive conjugated form, in which it naturally occurs in foodstuffs. Thus released, it enters into the growth of red cells. It probably similarly makes available some substance needed by nerve tissue, so far undetermined, which is not folic acid. Further study may identify such a substance. This point of view on the action of liver extract suggests that pernicious anemia is a complex type of cellular enzyme disturbance which the extract restores to normal with release of specific substances needed for normal red cell growth (pteroylglutamic acid) and for the normal nutrition of nerve tissue (a substance so far not identified).

RADIOACTIVE ISOTOPES IN TREATMENT OF LEUKEMIA AND POLYCYTHEMIA

Roentgen irradiation has long been the best available method for treating leukemia. It only slightly prolongs life, however, although the patient is made more comfortable by such therapy. Radioactive isotopes in recent years have been tried to replace roentgen therapy. Radioactive phosphorus, P^{32}, has been most widely used. The effect of this isotope is identical with that of other forms of irradiation. The only value claimed for it is the absence of radiation sickness. This is of no significance, however, in the hands of many radiologists who use small doses of roentgen rays. It has been suggested that no radioactive isotope should be used for treatment if the half-life is more than ten days because of possible unfavorable late effects from the long-continued irradiation. The half-life of radioactive phosphorus is 14.3 days. The occurrence of acute leukemia in patients with polycythemia treated with radioactive phosphorus raises the question of such possible ill effects. Even with the availability of P^{32} from Oak Ridge the drug remains expensive, requires special facilities for handling and is not generally available for clinical use. It has not been widely used but has been employed largely in research centers. More recently radioactive gold and manganese have been employed in the treatment of leukemia with much the same results as with P^{32}.

The use of radioactive isotopes has not greatly changed the outlook of the patient with leukemia. All patients eventually die from the disease. The average length of life in leukemia without any treatment is three years. With roentgen therapy the average is 3.5 years, and the patient is more comfortable. With radioactive phosphorus treatment the average is 3.6 years. The clinician should not feel that his patient is being deprived of an indispensable treatment if radioactive phosphorus is not available, provided roentgen therapy is used.

Other chemicals which have been found to have an effect similar to roentgen rays have been tried for leukemia. The nitrogen mustards have such an effect but are more valuable in Hodgkin's disease than in leukemia; even here, however, the effect is not remarkable. Urethane (ethyl carbamate) has been tried recently. This drug and nitrogen mustard were first used because they were found to cause leukopenia. When administered it has an effect much like roentgen irradiation but may cause nausea and vomiting. It is now being employed experimentally in many clinics. There is no evidence that it has any curative effect, but it may prove to be a valuable treatment for leukemia since it has few toxic effects, is readily available and is cheap. It may prove to be as valuable as roentgen irradiation in many cases. It is more effective in the myeloid than the lymphoid types of the disease.

In polycythemia the radioactive isotopes are probably the treatment of choice if readily available. The results with repeated venesections in this disease are most satisfactory, however, and so far the best alternative treatment. The effects with P^{32} are only temporary. There is no evidence that a patient lives longer with such treatment than with venesection. Only time can determine the place of such drugs in the treatment of polycythemia.

ABSTRACT OF DISCUSSION

PERNICIOUS ANEMIA WITH CORD SYMPTOMS

QUESTION (Dr. V. E. Lascara, Raleigh, N. C.): Given a case of pernicious anemia with spinal cord symptoms, what is the best therapeutic procedure?

ANSWER: A patient suffering from pernicious anemia with symptoms referable to the spinal cord requires more intensive treatment than with an anemia only. At the beginning 15 units of liver extract is given daily for two weeks. After this initial treatment 15 units is given twice weekly for three months. An injection of 15 units is then given weekly indefinitely, or at least until it is shown that no further improvement in the cord lesion is possible. This improvement may be slow, however, and may continue for a long period. A full diet including abundant meat, eggs, fruit and vegetables without an excess of carbohydrate should be insisted on. It is a question whether added vitamin B helps the cord lesion. It is a good procedure, however, to give a teaspoonful of dried brewer's yeast powder three times a day.

TREATMENT OF POLYCYTHEMIA

QUESTION (Dr. R. H. Clark, Hattiesburg, Miss.): Discuss further treatment of polycythemia.

ANSWER: Idiopathic polycythemia vera responds well to the administration by mouth or intravenously of radioactive phosphorus (P^{32}). This is available, however, only in larger centers. The final results of the treatment of polycythemia with this radioactive isotope will depend on the clinical course observed as the result of such treatment. Venesection is a satisfactory method of treating idiopathic polycythemia vera. The red cell mass (hematocrit reading times blood volume) is greatly increased in this disease and should if possible be determined in gaging treatment. A large amount of blood must be removed, depending on the level of the red cell mass. This is variable. It is safe to do venesections until the hematocrit reading shows 45 cc. of red cells per hundred cubic centimeters of blood.

CEREBRAL HEMORRHAGE

QUESTION (Dr. Sixto Y. Orosa, Bacolod, Philippines): Is it logical to use "dicumarol" or heparin in cerebral hemorrhage? Have cases been reported? Has folic acid been tried in leukemia? If so, with what results?

ANSWER: There is no reason to use heparin or "dicumarol" in cerebral hemorrhage. Folic acid has been tried in leukemia without success.

LEUKEMIA

QUESTION (Dr. Nathan Blumberg, Philadelphia): What is the value of urethane and nitrogen mustard in the leukemias and what is the usual life span after these drugs have been given to a patient with leukemia?

ANSWER: Both urethane and nitrogen mustard may help leukemia. These should be tried early in the course of the

disease or when the patient no longer responds to irradiation. The life span of patients with leukemia is so variable it is not possible to estimate this after the use of such drugs.

PERNICIOUS ANEMIA

QUESTION (Dr. P. Lancione, Bellaire, Ohio): Just how would you treat a patient with pernicious anemia?

ANSWER: A patient with pernicious anemia should be treated intensively at the beginning and adequately throughout his life. An excellent plan is as follows: 15 units of liver extract daily for the first two weeks, twice weekly for three months, weekly for three months, twice monthly for six months and monthly for the life of the patient.

CRUDE LIVER AND LIVER EXTRACT

QUESTION (Dr. Leslie S. Harrison, Flushing, N. Y.): Is crude liver better than liver extract for treatment of pernicious anemia?

ANSWER: It is doubtful whether crude liver extract is better than a refined preparation for the treatment of pernicious anemia. Some workers have thought that the cord lesions of pernicious anemia might be helped more by the crude extracts.

FOLIC ACID AND NEUROLOGIC RELAPSES

QUESTION (Dr. Morton S. Berk, Boston): What is the evidence that folic acid may cause an actual increase in the incidence of neurologic relapses in pernicious anemia?

ANSWER: Numerous workers have reported the development and progress of neurologic lesions in patients having intensive folic acid therapy. At times the lesions seem to develop explosively. There is no proof, however, that the incidence is greater. All agree with Dr. Tom Spies (Experiences with Folic Acid, 1947, Chicago, The Year Book Publishers, Inc., p. 82), however, that "It seems evident that folic acid does not always prevent the occurrence of combined system disease nor does it reverse the degenerative process once it has begun." These observations suggest that until more is known of the mode of action of folic acid in hemopoiesis and until a factor essential to the preservation of the central and peripheral systems is found, liver extract is the safest and most effective therapeutic agent for the routine treatment of pernicious anemia.

THE BLOOD PATTERN IN MALIGNANCY

QUESTION (Dr. Arthur H. Hopkins, Philadelphia): Will you give us your opinion of the value of "The Blood Pattern in Malignancy" as demonstrated and described by Dr. Leonard Bolen?

ANSWER: I have had no experience with this procedure.

USE OF NITROGEN MUSTARDS

QUESTION: Discuss the use of nitrogen mustards in the treatment of lymphatic diseases.

ANSWER: Many lymphoblastomas respond to treatment with the nitrogen mustards. If a lesion does not respond initially to irradiation it probably will not respond to nitrogen mustard, so roentgen irradiation seems the method of choice. After a patient's lesion has become resistant to irradiation it may respond, however, to the administration of nitrogen mustard, sometimes with restoration of sensitivity to irradiation. The greatest usefulness of nitrogen mustard so far is in Hodgkin's disease, in which the palliative results may be most striking. This drug is not a cure, however, any more than irradiation is a cure.

SECONDARY ANEMIA

QUESTION: What is the most effective way of treating secondary anemia?

ANSWER: The term "secondary anemia" is an unfortunate one. Earlier it was used to designate an anemia due to a known cause as opposed to "primary anemia" of unknown origin. In this sense both pernicious anemia and chlorosis were grouped together as primary anemia. Anemias due to hemorrhage, increased hemolysis, bone marrow aplasia, and bone marrow depression were classed as secondary. Every case of anemia should be studied carefully in the laboratory for evidence of increased hemolysis and for size and hemoglobin content of the red cell. Such data usually give a clue to the cause of the anemia. The clinical study of the patient should give other information. After determining the type and cause of anemia, treatment is simple, provided the cause can be removed or compensated for. If there is a low color index and/or volume index iron is indicated. This is best given as ferrous iron in adequate doses such as 9 to 15 grains (0.6 to 1 Gm.) daily.

FOLIC ACID

QUESTION (Dr. B. Spencer, Sterlington, La.): Does folic acid have a diuretic action?

ANSWER: No.

FOLIC ACID AND IMPULSE TRANSMISSION

QUESTION (Dr. George J. Boines, Wilmington, Del.): Has folic acid any effect on impulse transmission at the myoneural junction?

ANSWER: No.

THE EFFICACY OF FOLIC ACID

QUESTION (Dr. S. R. Blatteis, Brooklyn): What are the criteria indicating the efficacy of folic acid and is it advisable to continue the administration of folic acid at all during a remission in pernicious anemia?

ANSWER: Many workers have shown that macrocytic anemia due to a deficiency of the specific erythrocyte-maturing factor such as pernicious anemia responds dramatically to the administration of folic acid. The red cell count returns to normal and macrocytosis disappears. True pernicious anemia is due to a permanent deficiency of the specific factor, so must be treated throughout the life of the patient. Treatment should never be discontinued during a remission. Pernicious anemia is best treated with liver extract and not by folic acid alone.

FOLIC ACID IN MACROCYTIC ANEMIA

QUESTION (Dr. Paul W. Spear, Brooklyn): Is folic acid effective in the macrocytic anemias due to nutritional deficiency? Has it been tried in so-called achrestic anemia?

ANSWER: Folic acid is effective in the macrocytic anemia of sprue and the macrocytic anemia of childhood, both of which are due to a deficiency of the specific erythrocyte-maturing factor. There is much to suggest that folic acid is this specific factor. The term achrestic anemia has been used to designate a macrocytic anemia similar to pernicious anemia which does not respond to adequate liver therapy. It is doubtful whether there is a pernicious anemia which does not respond to liver. Achrestic anemia is probably not due to a deficiency of the specific erythrocyte-maturing factor and so would not be expected to respond to folic acid. A macrocytic anemia is present in liver disease, primary aplastic anemia, and in monocytic leukemia.

HYDROCHLORIC ACID NOT RECOMMENDED

QUESTION (Dr. J. P. Schaus Jr., Buffalo, N. Y.): In the treatment of pernicious anemia or other anemias associated with achlorhydria, does hydrochloric acid by mouth play a part?

ANSWER: The use of hydrochloric acid does not influence the results of treating pernicious anemia with liver and liver substitutes. It is unpleasant to take. There seems no indication for its use.

RUTIN THERAPY

QUESTION: What is the present status of rutin therapy?

ANSWER: Rutin is a glycoside which is said to be "effective in the treatment of conditions arising from high blood pressure associated with increased capillary fragility" (THE JOURNAL **131**:743 [June 29] 1946. Reports are conflicting, but it is doubtful whether capillary permeability is significantly influenced by the use of rutin.

RECENT ADVANCES IN THE TREATMENT OF PULMONARY DISEASES

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Without doubt the most important recent advance in the treatment of pulmonary diseases has been the use of antibiotics, especially the use of streptomycin in the treatment of pulmonary tuberculosis and its complications.

The following six organisms which cause an enormous amount of pulmonary disease either primarily or secondarily are highly sensitive to streptomycin in vitro:

Mycobacterium tuberculosis
Hemophilus influenzae
Hemophilus pertussis
Klebsiella pneumoniae
Pasteurella pestis
Pasteurella tularensis

It is further significant that with certain exceptions this in vitro sensitivity can be used and should be used as a good index of the possible effectiveness of the antibiotic in the treatment of infectious processes caused by these organisms.

Briefly I shall discuss: (1) the use of streptomycin in tuberculosis, (2) recent advances in the treatment of primary and secondary pulmonary diseases and (3) recent advances in the prevention of pulmonary diseases.

THE USE OF STREPTOMYCIN IN TUBERCULOSIS

If streptomycin were perfectly harmless, it could be given to every patient with active tuberculosis regardless of the nature and extent of the tuberculous disease and its complications. However, streptomycin is not perfectly harmless. This must not discourage us, since many of our most useful drugs are injurious if given unwisely.

Here let me say that although my personal experience with the use of streptomycin in tuberculosis has been meager, my experience with tuberculosis goes back forty years last month. The officers at Fitzsimons General Hospital have afforded me repeated opportunities to observe some of their cases. Moreover, John Barnwell, the physicians in the Veterans Administration and Corwin Hinshaw of the Mayo Clinic have given me the benefit of their experience with streptomycin.

In giving the public and the medical profession full information on what has been done with streptomycin in the treatment of tuberculosis, it is vitally important that neither the toxic effects nor the benefits be magnified on the one hand or minimized on the other.

About one thousand human beings with tuberculosis in one form or another have been treated with streptomycin. The most experienced men say that they have seen no patient who regretted taking the drug and no patient to whom they regretted giving the drug.

In what forms of tuberculosis should the drug be used? Without hesitation the drug should be given in tuberculous meningitis with or without miliary tuberculosis of the lungs. In days gone by, all these patients died. Today streptomycin will save a few to live possibly many years in good condition. Some will have their lives prolonged only months but will relapse and die after surprising temporary improvements; others will survive a varying period but with lingering signs and symptoms of serious damage by the disease to the central nervous system. A few will survive but with complete loss of hearing, which may be due to the disease, perhaps to the drug—time will tell. The ultimate fate of these patients with tuberculous meningitis treated with streptomycin cannot yet be told; thus far the majority relapse and die. More time for observation is necessary. The highly significant thing is that streptomycin gives such dramatic evidence of ability to control in a few instances this most fatal form of tuberculosis.

In treating meningitis the drug must be given both intramuscularly and intrathecally. Doses of 0.5 to 2 Gm. in the spinal canal have produced in a few hours complete paralysis of both lower extremities with paralysis of bladder and bowels. If the patient does not die of the meningitis, complete recovery from the paraplegia with return of normal function of both bladder and bowels are to be expected. Even with the purest forms of streptomycin now available, not more than 100 mg. should be given daily intrathecally. The recommendations of the experts vary from 10 to 100 mg. I again remind you that we are dealing with a hitherto invariably fatal form of tuberculous disease. Unavoidable bad effects of the drug must be tolerated if useful life can be saved. Miliary tuberculosis of the lungs without meningitis responds sometimes even more dramatically than meningitis.

A number of patients with oral and pharyngeal tuberculous lesions, ominous complications, have completely healed these distressing local forms of the disease with streptomycin by intramuscular injection with or without streptomycin inhalations.

Tuberculous laryngitis and tracheobronchitis also seem amenable to streptomycin.

In general, the indications in pulmonary tuberculosis are to give the drug to patients with early, acute exudative lesions which are progressing despite good treatment along orthodox lines. Acute spread to the contralateral lung after thoracoplasty would seem to be a prime indication. Ordinary chronic fibroulcerative tuberculosis with much fibrosis and cavity formation is not responsive to the drug. Streptomycin shows little or no effect on the caseous necrotic lesions, which are later often the cause of relapse. Collapse therapy and bed rest still play indispensable roles in treatment.

Finally, two questions must be answered. First, can streptomycin be given in effective doses and not at the same time render the patient for an indefinite period more or less deaf? The answer is yes, provided that by frequent audiometric determinations one catches the earliest sign of damage to hearing and stops the drug. How much good will have been done the patient by this time is unpredictable. The experts agree that deafness is not a serious or frequent toxic effect.

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The second and more important question is not so easily answered. Can streptomycin be given in remedial doses and not make life for the patient more or less miserable if not hazardous for an indefinite period because of damage to the sense of equilibrium? More experience is needed before final answer can be given to this question. Some of the experts are frankly pessimistic, while others are hopeful that one way or another damage to the vestibular branch of the eighth nerve can be avoided or minimized.

Basic requirements for the intelligent use of streptomycin in tuberculosis are adequate clinical experience with the natural history of the disease and its often surprising variations and a knowledge of its pathology. Thus fortified the clinician will know when to step in with streptomycin to the best advantage of his patient.

As to the future of "antibiotic" therapy in tuberculosis, four possibilities exist: (1) that streptomycin will be altered by the chemists' retaining and even enhancing its antibiotic effects but getting rid of its peculiar and specific neurotoxic effect; (2) that combined or alternating use of streptomycin with other antibiotics against the tubercle bacillus may be more helpful than treatment with one antibiotic alone; (3) that clinicians can arrange a dose schedule or method of administration by which damage to the eighth nerve can be avoided even if the chemists cannot improve the drug, and (4) that a new, safer and more potent antibiotic against the tubercle bacillus may be discovered.

PRIMARY AND SECONDARY PULMONARY CONDITIONS

Of fundamental importance to good chemotherapy of pulmonary diseases are: (1) identification of the organism causing the infectious process; (2) determination of its sensitivity to one or more antibacterial agents (penicillin, streptomycin, sulfonamide drug, etc.); (3) repeated tests, especially in chronic pulmonary diseases, for changes in bacterial resistance and predominant flora, and (4) timely blood cultures.

As to methods of antibiotic therapy, aerosols have their advocates but the preferred method nearly always is intramuscular injection. Aerosols are troublesome, often irritating to the mouth and throat and certainly not as effective.

Taplin and Bryan of Rochester, N Y. have devised apparatus and a method for the production and inhalation of micronized antibacterial agents. This method of administration awaits adequate clinical trial.

Tularemic pneumonia, recognized early, is the ideal disease to treat with streptomycin.

Hemophilus influenzal infections of the respiratory tract respond well to combinations of sulfadiazine and streptomycin. Acute inflammation of the epiglottis due to this organism with obstruction of the airway requires tracheotomy and sulfadiazine.

Pneumonia due to Klebsiella pneumoniae must be recognized early and treated vigorously with streptomycin.

The pneumonitis that formerly progressed to abscess of the lung, if recognized early and treated vigorously with both sulfonamide drugs and penicillin, may resolve without formation of cavity.

Since Pasteurella pestis is highly sensitive to streptomycin, it may be hoped that streptomycin will save some of the patients with pneumonic plague.

Aspiration pneumonitis may be prevented or cured by timely and skilful bronchoscopic aspirations of retained secretions plus the use of penicillin.

The combined use of sulfonamide drugs, penicillin and streptomycin parenterally, by intratracheal instillation and by inhalation will not alter the irreversible changes of chronic bronchiectasis but will make unavoidable lobectomy safer. Without doubt chemotherapy has made thoracic surgery almost as safe as abdominal surgery.

I direct your attention to the statement made by Bryan Blades that in World War II the death rate of troops from chest wounds was the lowest ever recorded in the history of warfare. Blades said that the reduction in mortality rate from 24.5 per cent in World War I to 8.1 per cent in the recent conflict was due not so much to technical improvements but to skilful preoperative management and judicious timing and selection of surgical procedures.

Mention should be made here of the Blalock-Taussig and other operations for the improvement of deficient circulation to the lungs and the transformation of the pulmonary-circulatory invalid with congenital heart disease into a reasonably well person.

PREVENTION OF PULMONARY DISEASE

A. Immediate Prevention.—Here should be mentioned once more the use of sulfonamide drugs and penicillin (1) to prevent postoperative pulmonary complications, especially after thoracic surgery and (2) to prevent aspiration pneumonitis; the use of streptomycin to prevent acute tuberculous spread to the other lung after thoracic surgery; the use of anticoagulants or venous ligation or both to prevent pulmonary embolism.

Your attention is again directed to the poliomyelitis exhibit of A. B. Baker and the Minneapolis group. In the treatment of certain forms of bulbar poliomyelitis, they have shown the great value of timely tracheotomy, judicious aspiration of bronchial secretions, the avoidance of hypoxia and the use of penicillin in the prevention of pulmonary complications.

B. Remote Prevention.—1. Vaccination against influenzal viral infections is promising. 2. This country has been slow to approve BCG (bacillus Calmette Guérin) vaccination against tuberculosis. At least two medical schools in this country are using BCG to protect medical students and nurses. Before this decade runs out it seems likely that highly exposed groups and highly susceptible sections of our population will be offered the protection against tuberculosis that is promised by BCG vaccination.

CONCLUSION

Universal and conscientious application of the following four procedures will powerfully assist the campaign against tuberculosis: (1) mass roentgen examination of entire communities; (2) routine roentgenograms of the chests of those admitted to general hospitals; (3) more frequent sputum examinations by general practitioners, and (4) BCG vaccination of highly exposed groups and highly susceptible sections of our population. Only recently has the importance of these procedures become adequately appreciated.

ABSTRACT OF DISCUSSION

MINIMAL TUBERCULOSIS AND STREPTOMYCIN

QUESTION: Why not treat minimal tuberculosis with streptomycin?

ANSWER: At present—please note that I emphasize at present—physicians with the largest experience with the use of streptomycin are unwilling to use streptomycin in the treatment of minimal pulmonary tuberculosis for the following reasons: 1. The vast majority of these patients will get well without streptomycin. 2. The drug is toxic and the immediate and remote bad effects are not accurately predictable. 3. The development of "bacterial resistance" may leave the patient with an incompletely eradicated infection due to an organism now highly resistant to streptomycin. Ninety-five to 97 of 100 patients with minimal pulmonary tuberculosis will get well with the usual orthodox treatment without streptomycin. Don't shoot at a dickeybird if shooting will leave you with empty gun in the path of a tiger! It is impossible at the onset of their disease to predict which of the hundred will be the 3 or the 5 patients who will do badly and should have streptomycin to prevent spread of their disease. If the drug were perfectly harmless it could be given to all and accurate prophecy would be of no importance. Unfortunately practically every patient taking 2 Gm. of streptomycin daily for three to four weeks will have damage to vestibular function and a few may become more or less deaf. Improvement in the drug, modifications of dose schedule or methods of administration or combination with another antibacterial agent or discovery of a safe, more potent antibiotic may make it possible to use chemotherapy for every patient with tuberculosis. It may be overoptimistic to say that this day is close at hand! As for "bacterial resistance," this is a disturbing phenomenon which is being studied intensively.

HOME TREATMENT WITH STREPTOMYCIN

QUESTION: Can streptomycin be used in the home for treatment of tuberculosis?

ANSWER: The best place (the only place according to experts) for a tuberculous patient taking streptomycin is in the hospital or sanatorium under the supervision of a physician competent in diseases of the chest and experienced in the use of streptomycin. It can be formidable if not impossible to treat a patient with tuberculous meningitis in his home. Since intrathecal injections of streptomycin frequently cause temporary paralysis of bladder and bowels the difficulties of the nursing problem at home would be multiplied. It is also difficult to imagine a patient able to pay for 2 Gm. of streptomycin daily and at least two visits daily by his physician and nursing care besides and not able to go to a hospital. Tuberculous adenitis with or without sinus, all tuberculous fistulas, tuberculosis of the mouth, pharynx and larynx and acute tuberculous spread in the lungs all could be treated at home if absolutely necessary. Certainly, if a patient could not pay for sanatorium care and streptomycin but could pay for streptomycin only, I would give him his chance at home. In view of the serious disturbance of equilibrium which may result from streptomycin, no physician should undertake to use streptomycin in tuberculosis without sufficient preparation. He must have (1) adequate experience with diseases of the chest; he must have (2) studied the scientific exhibits on streptomycin at this hundredth anniversary of the American Medical Association; he should have (3) conferred with those who have used the drug in the treatment of tuberculosis, and (4) he should have familiarized himself with the published reports on the use of streptomycin. I recommend particularly (1) Carl Muschenheim's fine article "The Streptomycin Treatment of Tuberculosis" (*New York Med.* **3**:17 [May 20] 1947); (2) T. F. Paine, R. Murray and M. Finland: "Streptomycin: I. Bacteriologic and Pharmacologic Aspects; II. Clinical Uses" (*New England J. Med.* **236**:701 and 748 [May 8 and May 15] 1947), and (3) "Symposium on Streptomycin" (*Am. J. Med.* **2**:419 [May] 1947).

MICRONIZED THERAPEUTIC AGENTS

QUESTION: What is the micronized method of giving antibiotics?

ANSWER: In *Science* for May 9, 1947 will be found an article "Administration of Micronized Therapeutic Agents by Inhalation or Topical Application" by George V. Taplin and Fred A. Bryan of the University of Rochester, Rochester, N. Y. Taplin and Bryan have devised apparatus for the grinding of certain therapeutic agents to a very fine or "micronized" state. They have also devised the apparatus for the administration of this finely ground powder by inhalation. Although this method has not yet had adequate clinical trial, preliminary reports indicate that therapeutic concentrations in the blood may be easily secured and maintained. The clinical and bacteriologic responses to this treatment have been excellent in more than 40 cases of various diseases in which penicillin therapy was indicated. Taplin and Bryan stated that patients prefer this type of treatment to either intramuscular injections or aerosol inhalations. Of further interest is that local sensitivity reactions to penicillin in the last 35 cases were eliminated by the incorporation of 2 to 5 mg. of finely ground diphenhydramine hydrochloride in each dose of penicillin. If it will be possible to give streptomycin by this method in smaller but effective doses to tuberculous patients, it would prove a most important discovery.

MEDIASTINAL LYMPHADENOPATHY

QUESTION: What course of therapy would you pursue for patients who have undiagnosed bilateral mediastinal lymphadenopathy?

ANSWER: Exploration of the chest by an experienced thoracic surgeon is just as safe as exploration of the belly by an average surgeon. In other words, exploratory thoracotomy is not yet quite as safe in average hands as exploratory laparotomy. Sulfonamide drugs, penicillin and streptomycin have certainly reduced the risk, however. Note Meade's recent report of 236 lobectomies with only one death. My colleague, Col. John B. Grow of Denver, who is a skilled thoracic surgeon, is convinced that it is unwise, unscientific and unjust to make a diagnosis of Hodgkin's disease on the basis of presumed favorable response to irradiation of the mediastinum. He thinks it much better to do a diagnostic mediastinotomy and secure a piece of tissue or gland for diagnosis. The well known tendency of Boeck's sarcoid to improve spontaneously is one source of error. Perhaps he is right, but the fact remains that occasionally the surgeon is unable to make a diagnosis without removing the lung or a lobe of the lung, with the result that a major operation is done unnecessarily. Since five year cures of cancer of the lung after pneumonectomy are very few, and since it is likely that late diagnosis is partly responsible for this discouraging state of affairs, both surgeon and physician must collaborate to secure earlier diagnosis. More frequent diagnostic thoracotomy offers one way of arriving at an early diagnosis. In this matter of early diagnosis of malignant diseases of the lung, I would urge the importance of three most useful procedures: (1) roentgen examination of the chest of every patient admitted to a general hospital; (2) more frequent resort to bronchoscopic examination, and (3) examination of fresh sputum obtained at bronchoscopic examination for tumor cells and incidentally for tubercle bacilli.

CARCINOMA OF LUNG

QUESTION: Under what circumstances would you recommend surgical treatment of carcinoma of the lung?

ANSWER: I am pessimistic about the prognosis of cancer of the lung even when the diagnosis has been made early and even when the surgeon is very experienced. At this date the five year cures after surgery are no more than 5 per cent. This figure should be greatly improved with increasing knowledge of diseases, greater uses of the roentgen ray and improved methods of diagnosis such as staining bronchial secretions for tumor cells.

STREPTOMYCIN IN ACTIVE TUBERCULOSIS

QUESTION: What is the place of streptomycin in the treatment of the usual case of active pulmonary tuberculosis?

ANSWER: Streptomycin should be used in the early acute exudative types of pulmonary tuberculosis. The patient will be subjected to unnecessary risks and expense if streptomycin is given for the usual fibroulcerative case of pulmonary tuberculosis. At this time, streptomycin cannot be recommended for the treatment of (1) minimal pulmonary tuberculosis, (2) chronic fibroid or fibrocaseous pulmonary tuberculosis, (3) acute destructive and apparently terminal types of pulmonary tuberculosis or (4) chronic tuberculous empyema.

TUBERCULOSIS SANATORIUMS

QUESTION (Dr. George J. Boines, Wilmington, Del.): Do you advise the use of streptomycin for general use in state tuberculosis sanatoriums?

ANSWER: It all depends on what you mean by "general use." I think that streptomycin should be available for selected cases in all tuberculosis sanatoriums.

TUBERCULOUS SINUS

QUESTION (Dr Victor Siegel, Red Banks, N. J.): Can streptomycin be used for tuberculous empyema sinus?

ANSWER: Many cases of tuberculous sinus are improved by streptomycin. How much good will result from the use of streptomycin in "tuberculous empyema sinus" will depend on the size and pathologic state of the empyema pocket and also on the state of the underlying pulmonary parenchymal disease.

FAILURE OF STREPTOMYCIN IN EMPYEMA

QUESTION (Dr. Alexander Tish, Washington, D. C.): Why has streptomycin intrapleurally been of little or no value in tuberculous empyema and how can the failure be explained?

ANSWER: Streptomycin is of little or no value in tuberculous empyema because of the pathologic nature of this serious complication of pulmonary tuberculosis. It must be understood that streptomycin is helpful in early acute exudative pulmonary tuberculosis and has little or no effect on caseating lesions. It seems likely that in tuberculous empyema innumerable small as well as large caseating lesions are located in the pleura and in the underlying lung. Hinshaw thinks that the p_H of the empyema fluids may interfere with the bacteriostatic action of the drug.

HOW TO AVOID BAD EFFECTS OF STREPTOMYCIN

QUESTION (Dr. Sixto Y. Orosa, Bacolod, Philippines): Kindly suggest a plan for the administration of streptomycin for the treatment of pulmonary tuberculosis to avoid the bad effects on the patient.

ANSWER: In answering this question I should like it clearly understood that the suggested dose schedule has not been used long enough either to prove its efficacy or its harmlessness. I am convinced that daily doses of 2 Gm. for a period of one hundred and twenty days is too much. It seems possible already from animal experiment and clinical trials that a smaller daily dose in an intermittent schedule may be both effective and harmless. Suggested schedule of treatment: 1. Give 200 mg. of streptomycin intramuscularly every three hours; begin at 6 a. m., and give five doses in the twenty-four hours; not more than 1 Gm. daily. 2. Follow this schedule for two weeks; then stop for one week. Resume for two weeks, and stop for one week. 3. This schedule may be repeated for approximately one hundred and twenty days of actual administration of the drug. Time will tell whether this length of time and dose are optimal.

TUBERCULOSIS OF THE SKIN

QUESTION (Dr. Michael Margolies, Coatesville, Pa.): Is streptomycin of value in treating tuberculosis of the skin?

ANSWER: Experience is lacking to give adequate answer to this question.

"PROMIN" FOUND WANTING

QUESTION (Dr. S. A. Bolosky, Philadelphia): Has "promin" (sodium p,p-diaminodiphenylsulfone-N,N'-didextrose sulfonate) by injection or "promizole" (4,2-diaminophenyl-5'-thiazolylsulfone) by mouth been given a long enough trial in pulmonary tuberculosis?

ANSWER: It is possible that combinations of streptomycin with another antibacterial agent such as "promin" or "promizole" may be more effective than the use of streptomycin or "promin" or "promizole" alone. A combination of streptomycin with some other bacterial agent may have the advantage of permitting the use of smaller and less toxic doses of streptomycin. Much work needs to be done on the synergistic action of antibacterial agents. "Promin" by injection and "promizole" by mouth have been weighed clinically and found wanting.

WHAT'S NEW IN ENDOCRINOLOGY

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The object of this paper is to discuss the more important therapeutic advances that have occurred recently in the field of endocrinology. The most significant contributions have perhaps been those dealing with the use of antithyroid drugs and radioactive iodine in the treatment of toxic goiter and those dealing with the relation of androgens and estrogens to carcinoma of the prostate and breast respectively.

THE PITUITARY

Anterior Lobe.—Our knowledge of pituitary function has increased still further. Interesting developments have been the isolation in Evans' laboratory in the University of California of an adrenocorticotropic hormone and of a purified growth hormone. Preliminary reports on the effects of the adrenocorticotropic hormone are contradictory. According to Thorn and others [1] it caused stimulation of all the known functions of the adrenal cortex in 2 patients with pronounced hypopituitarism. According to other observers [2] it does not affect the excretion of sodium and chloride. Further observations will be necessary to determine the precise status of this material. It is available at the present time for experimental use in only a few laboratories. Addison's disease is sometimes caused by atrophy of the adrenal cortex as a result of inadequate stimulation by the anterior lobe of the pituitary. On theoretical grounds it would be desirable to treat the disease in such instances with a suitable pituitary extract. No evidence is yet available as to whether prolonged administration of adrenocorticotropic hormone results in the development of antibodies which inhibit its effect. Most pituitary extracts available in the past have not been suitable for routine clinical use because of the temporary nature of their action. Preparations of the thyrotropic hormone will temporarily cause an

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1. Forsham, P. H.; Thorn, G. W.; Prunty, F. T. G., and Hills, A. G.: Clinical Studies with Pituitary Adrenocorticotropin, J. Clin. Endocrinol., to be published.

2. Mason, H. L.; Power, M. H.; Rynearson, E. H.; Ciaramelli, L. C.; Li, Choh H., and Evans, H. M.: Results of Administration of Anterior Pituitary Adrenocorticotropic Hormone to a Normal Human Subject, J. Clin. Endocrinol., to be published.

increase in basal metabolism in many patients in whom there is any thyroid tissue capable of function. The metabolism always returns to its initial level or even a lower level with prolonged administration. The longest period of increase in basal metabolism which I have observed in man during the administration of thyrotropic hormone has been nine weeks.

Some of the newer preparations of pituitary gonadotropin in powder form have caused some stimulation of ovarian function. In a few women with secondary amenorrhea it has been possible to induce menstruation and in a few women with anovulatory menstrual cycles it has been possible to induce ovulation.

The new preparation of the growth hormone developed by Evans is of interest but so far has not been tried adequately in man. Preparations of the growth factor available up to the present have not proved very effective in clinical medicine. Engle and others [3] have observed temporary growth in a pituitary dwarf with a preparation of the growth factor.

The observations of Markee, Sawyer and Hollinshead [4] that the hypothalamus plays a major role in the release of luteinizing hormone from the anterior lobe of the hypophysis is of importance because of the influence that neurogenic factors appear to play in the control of endocrine function.

Multiglandular Deficiencies Secondary to Hypopituitarism.—In patients showing decided loss of pituitary function such as those with chromophobe adenoma of the pituitary and hypopituitary cachexia (Simmonds' disease) evidence has been obtained of the presence of hypothyroidism, hypofunction of the adrenal cortex and hypogonadism. Thus patients with chromophobe adenoma of the pituitary may show a very low level of basal metabolism, a low blood pressure, reduction in the concentration of sodium in the serum, increase in the secretion of sodium in the urine, reduction in the fasting blood sugar and various evidences of hypogonadism, including atrophy of the genitalia, amenorrhea and impotence. Patients with pronounced hypopituitarism sometimes show typical addisonian crises which have to be treated with the parenteral administration of large doses of adrenal cortex extract and the intravenous administration of sodium chloride and dextrose. They also suffer from attacks of hypoglycemia which are difficult to distinguish from addisonian crises. Patients with deficiency of the adrenal cortex secondary to hypopituitarism do not appear to become pigmented as frequently as patients with Addison's disease caused by destruction of the adrenal glands.

Posterior Lobe.—A few interesting reports have appeared on the posterior lobe of the pituitary, but no outstanding advances have been made. The most practical development has been further demonstration of the fact that diabetes insipidus may be controlled satisfactorily either by insufflation of posterior pituitary powder into the nasal cavities or by the intramuscular injection of "pitressin tannate in oil."

THE THYROID; TOXIC GOITER

Three important developments have occurred in the treatment of toxic goiter: (1) irradiation of the pituitary, (2) the use of antithyroid drugs and (3) the use of radioactive iodine.

3. Engle, E. T., and others: Personal communication to the author.
4. Markee, J. E.; Sawyer, C. H., and Hollinshead, W. H.: Activation of Anterior Hypophysis by Electric Stimulation in the Rabbit, Endocrinology 38:345-357 (June) 1946.

Irradiation of the Pituitary.—A close relationship exists between the anterior lobe of the pituitary and the thyroid. The following effects of administration of the thyrotropic hormone have been observed in man: (1) increase in basal metabolism in all patients except those with complete myxedema; (2) production of thyrotoxicosis in patients with nontoxic goiter; (3) production of a syndrome resembling exophthalmic goiter in patients with a normal or slightly subnormal level of basal metabolism, and (4) increase in the severity of toxic goiter.

As has been pointed out, the increases in basal metabolism have always been temporary and have disappeared with continued administration over a period of eight to nine weeks. In a few patients with exophthalmic goiter, prolonged administration appears to have resulted in a cure. Following the initial increase, the basal metabolism has dropped to the normal level and remained there. Exophthalmos has not been reported in man as a result of the administration of the thyrotropic factor but it has been observed in various experimental animals. Hyperthyroidism secondary to hyperpituitarism has been noted in some patients with acromegaly, and hypothyroidism secondary to hypopituitarism has been noted in patients with chromophobe adenomas of the pituitary and in those with Simmonds' disease and anorexia nervosa.

The evidence available supports the hypothesis that the thyroid is only one link in the chain of events leading to the development of the symptom complex known as toxic goiter. Overstimulation by the pituitary appears to be an important factor. The cause of the stimulation of the pituitary has not been definitely determined but is probably related to some disturbance in the hypothalamus. Attempts to treat the disease by removing or destroying the thyroid probably do not attack the fundamental cause.

I have attempted to apply the knowledge of the pituitary-thyroid interrelations by irradiating the pituitary in a series of 43 patients with toxic goiter. A permanent remission was produced in about one third of them. These observations are of great importance from the standpoint of the mechanism which may be involved in the development of toxic goiter. However, it is not recommended that irradiation of the pituitary be used for the routine treatment of toxic goiter at the present time, chiefly because the percentage of cures is too low. Theoretically, this treatment might result in damage to other functions of the pituitary and to important structures in the base of the brain above the pituitary. Several years have now elapsed since these patients were treated and so far untoward early or late complications have not been observed.

Antithyroid Drugs.—Thyroidectomy, antithyroid drugs and radioactive iodine affect the thyroid directly and probably do not attack the underlying cause of the disease. In actual practice, control of the thyrotoxic phase of toxic goiter has proved to be a satisfactory form of treatment. The two antithyroid drugs most commonly used have been thiouracil and propylthiouracil. Propylthiouracil produces fewer toxic reactions than thiouracil but is not free from danger. These drugs have been used in two ways, namely, to treat the disease medically and to prepare patients for operation.

Medical Management: Sufficient time has not yet elapsed to determine the percentage of cures produced by thiouracil and prophylthiouracil. The evidence available indicates that when the basal metabolism is maintained at the normal level with these drugs for periods of nine to twelve months, no recurrence of the disease is noted after omission of treatment in about 60 per cent of patients. The percentage of cures appears to be related to the length of time that the basal metabolism is maintained at the normal level before treatment is discontinued. The longer the drug is administered the higher the percentage of cures. Patients who are not cured by an initial course of treatment may show disappearance of the disease following a second or third course. Great caution must be used in concluding that toxic goiter has been cured by drug therapy because of the tendency of the disease to show spontaneous remissions and relapses and the observations of recurrence of the disease after many months of drug therapy. It will take several more years to determine the percentage of cures following adequate periods of administration. The development of these drugs represents an important advance in the treatment of toxic goiter, but they are not the final answer to the problem. In order for a drug to be satisfactory for medical management it must produce a cure in nearly all patients without producing toxic reactions. It is desirable to continue the observations already begun on the medical management of the disease in order to obtain more precise data on the percentage of cures. It is generally agreed that antithyroid drugs are valuable in the treatment of persistence and recurrence of toxic goiter following subtotal thyroidectomy and in the treatment of patients who present poor surgical risks; e. g., some older patients with cardiac decompensation.

Surgical Management: The introduction of antithyroid drugs, particularly propylthiouracil, represents an important advance in the preoperative preparation of patients with toxic goiter. With these drugs it is possible to eliminate the thyrotoxicosis completely in most instances, whereas iodine usually controls the disease only partially. Propylthiouracil is of the greatest value in the preoperative preparation of patients who have thyrotoxicosis in severe form, and these are the patients who have presented the most serious operative risks. With proper preparation, the mortality from thyroidectomy for toxic goiter has dropped almost to the vanishing point. Hospitalization of patients during the preoperative period is not necessary except in the presence of a crisis or some complication such as cardiac decompensation. Propylthiouracil is given until the basal metabolism drops to within normal limits. Iodine is then administered in addition to propylthouracil for one week preceding operation in order to reduce hyperplasia and the danger of oozing of blood at the time of operation. Throughout the preoperative period the patient is given a diet high in calories. Operative procedures may be carried out a few days after admission to the hospital, thus greatly reducing the cost of hospitalization. Propylthiouracil may be discontinued at the time of operation but the administration of iodine is kept up until discharge from the hospital.

Radioactive Iodine.—The use of radioactive iodine represents an ingenious attack on the thyroid itself in patients with toxic goiter. Thyroxine contains 65 per cent of iodine by weight. When small amounts of iodine are administered, the iodine is taken up almost entirely by the thyroid gland and, if radioactive, destroys many of the thyroid cells. An end result of such therapy is the development of areas of fibrosis in the thyroid gland. Myxedema may be caused by the administration of radioactive iodine to experimental animals. When given to patients with toxic goiter in proper amounts, it produces a cure in a large percentage of patients. As improvement sets in, the thyroid gland decreases in size. Patients receiving this form of treatment have not yet been followed long enough to determine the percentage of cures and the incidence of late complications, if any. No instance of carcinoma has been reported among patients followed up to the present time. In a few patients some temporary hoarseness has developed. Seidlin, Marinelli and Oshry[5] have recently reported striking improvement in a patient with hyperfunctioning metastases of adenocarcinoma of the thyroid. However, most carcinomatous cells do not produce much thyroxine and take up little radioactive iodine. This material is, therefore, not of much value in most patients with carcinoma of the thyroid.

Malignant Exophthalmos.—In most patients with exophthalmic goiter the prominence of the eyes becomes grossly less when the basal metabolism is reduced to the normal level. In a few instances the prominence of the eyes continues to increase in spite of adequate control of the thyrotoxicosis. Some observers are of the opinion that this phenomenon is more apt to occur if the basal metabolism is subnormal. The exophthalmos sometimes becomes so pronounced that it is impossible to protect the eyeball by closing the lids. Increase in the prominence of the eyes in spite of a normal or subnormal metabolism indicates that the cause of the disease is still active. Exophthalmos has been produced in experimental animals with thyrotropic factor from the pituitary. Dobyns[6] has recently described the organic changes in the orbit associated with the administration of thyrotropic factor to animals.

The treatment of malignant exophthalmos is unsatisfactory. Radical measures should be employed only when it is impossible to avoid complications with medical treatment, which includes the combined administration of iodine and desiccated thyroid and irradiation of the pituitary. Surgical relief of malignant exophthalmos involves removing part of the orbit, usually the roof and part of the lateral wall. Most surgeons are not enthusiastic about the results of surgical intervention.

THE PARATHYROIDS

Several interesting reports have appeared on the parathyroids but no really new developments have occurred. Parathyroid tetany is now a relatively infrequent complication of thyroidectomy and its treatment has been perfected. It has been clearly demonstrated that if this disorder is treated adequately as soon as it is recognized, it does not reduce life expectancy and complications such as bilateral cataracts do not develop. Small doses of dihydrotachysterol supplemented with

5. Seidlin, S. M.; Marinelli, L. D., and Oshry, E.: Radioactive Iodine Therapy: Effect on Functioning Metastases of Adenocarcinoma of the Thyroid, J. A. M .A. **132**:838-847 (Dec. 7) 1946.

6. Dobyns, B. M.: Studies on Exophthalmos Produced by Thyrotropic Hormone: Changes Induced in Various Tissues and Organs (Including Orbit) by Thyrotropic Hormone and Their Relationship to Exophthalmos, Surg., Gynec. & Obst. **82**:609-617 (May) 1946.

calcium salts by mouth provide the best form of treatment. Vitamin D in large doses is also effective in promoting absorption of calcium salts from the gastrointestinal tract and may be employed in the treatment of parathyroid tetany if dihydrotachysterol is not available.

THE ADRENALS

Some progress has been made in the development of new synthetic products which substitute for the adrenal cortex. The synthetic material desoxycorticosterone acetate affects sodium and potassium metabolism but not carbohydrate metabolism. In the form of pellets implanted subcutaneously it has proved to be a fairly satisfactory method of treatment. Not all patients tolerate the material well, and in them it is necessary to use adrenal cortex extract. Other products, such as 11-dehydrocorticosterone, are not available commercially but there is reason to believe that a synthetic product will soon be available that will affect sodium, potassium and carbohydrate metabolism. Sufficient data have now been collected to demonstrate that patients with Addison's disease may be kept alive for long periods of time. They do not have much reserve and are in great danger of having serious intercurrent infections at any time.

It has been my policy to rely on adequate substitution therapy with adrenal cortex extract or desoxycorticosterone acetate. Patients periodically have crises in spite of treatment that is adequate to maintain them under most circumstances. The reason for the failure is not clear. The maintenance requirement of patients varies greatly and their susceptibility to crises also shows great variation. When pellets of desoxycorticosterone were first used in treatment it was considered necessary to determine the maintenance requirement of patients by daily injections of this material. From the figure thus obtained for maintenance purposes, the known rate of absorption of this material from each pellet and the percentage of material supposed to be eliminated unused when it was given once a day by injection, it was possible to calculate roughly the number of pellets required for the initial implantation. It is now known that this procedure is impractical because pellets from different manufacturers vary in their rate of absorption. It is common practice at the present time to implant initially in the subcutaneous areolar spaces four pellets of 75 mg. each, or a total of 300 mg. If this amount is not adequate, additional pellets are implanted in increments of 150 mg. In most patients the initial implantation does not need to exceed 450 mg., but a few require as much as 600 mg. Before implanting pellets it is necessary to determine the response of patients to the daily parenteral administration of desoxycorticosterone acetate. A few patients do not tolerate this material well. Complications of its use are the development of hypertension, edema which may be generalized and the production of focal areas of necrosis in cardiac and skeletal muscle. These areas of necrosis in the heart muscle may so impair the circulation that death results.

Some progress has been made on the site of formation of the various principles of the adrenal cortex. Androgens are apparently produced in the reticular zone, while the cells of the outer layer appear to be devoted to the control of sodium and potassium metabolism. Numerous observations have appeared on the determination of 17-ketosteroids in the urine in health and disease. In patients with Addison's disease the production of 17-ketosteroids is low because of destruction of the glands.

THE TESTES

Hypofunction.—Observations previously reported on the treatment of hypogonadism have been extended and confirmed. Chorionic gonadotropin has proved to be a satisfactory agent for stimulation therapy and testosterone propionate for substitution therapy. Chorionic gonadotropin will produce maximum stimulation of function only when the testes are capable of showing maximum response to stimulation. Persistence of hypopituitarism for a period of several years may result in irreparable damage to the testis so that it can no longer show a maximum response to stimulation. Under these circumstances, it is necessary to use testosterone propionate in order to produce the greatest possible change. One of the most important considerations in hypogonadism beginning early in life is the correct age for starting treatment. Treatment should be started at the age at which puberty normally sets in in order to insure maximum growth of the genitalia and prevent the skeletal abnormalities associated with hypogonadism. The male sex hormone will cause growth of the genitalia at any age in patients with a pronounced deficiency but the genital growth is not as great after as during the age of puberty. The uses and misuses of testosterone propionate have been discussed in a previous communication to this journal.[7] It is contraindicated in older men in whom the presence of carcinoma of the prostate is suspected.

Sterility.—A great deal of interest has developed on the subject of sterility. The male is sterile in infertile marriages in about 20 per cent of the patients. Stimulation of spermatogenesis in patients with secondary hypogonadism is not very satisfactory. In a few instances it is possible to cause some stimulation with some of the newer pituitary gonadotropins prepared in powder form. In determining the cause of sterility, it is advisable to investigate the male first, because it is comparatively easy to make a careful study of the production of spermatozoa.

THE OVARIES

Menstruation.—Knowledge of ovarian function has gradually increased. Rossman and Bartelmez[8] have recently reported that few women menstruate regularly at twenty-eight day intervals. Fluctuations of one to five days are to be expected, and the twenty-eight day period occurs only once in ten times. An unusually long or short cycle may occur at any time in any normal woman. Observations on the female macaque have indicated that preovulatory and postovulatory phases of the cycle vary independently of one another and that ovulation may occur at any time in either a long or a short cycle. Sevitt[9] has also demonstrated that ovulation may occur at any time in the first half of the cycle, even during the latter part of menstruation. These observations clearly show that the calculation of the so-called safe period on the basis of the expected date of the next menstrual period is unreliable.

7. Thompson, W. O.: Uses and Abuses of the Male Sex Hormone, J. A. M. A. **132**:185-188 (Sept. 28) 1946.
8. Rossman, I., and Bartelmez, G. W.: Delayed Ovulation: Significant Factor in Variability of the Menstrual Cycle, Am. J. Obst. & Gynec. **52**:28-33 (July) 1946.
9. Sevitt, S.: Early Ovulation, Lancet **2**:448-450 (Sept. 28) 1946.

There has been some development in pregnancy tests, although the Friedman modification of the Aschheim-Zondek procedure continues to be the most satisfactory method for routine clinical use.

An interesting observation has been the demonstration of changes in the early morning temperature during various phases of the menstrual period. In the premenstrual phase the temperature falls one or two days before the onset of menstruation. It falls further in the menstrual phase, sometimes to as low as 97 F., and then rises to between 98 and 99 F. In the follicular phase the temperature fluctuates between 98.4 and 99 F., and in the ovulatory phase it falls suddenly, usually about the fourteenth day before the onset of the next flow. It sometimes falls to as low a level as 97 F. and then rises suddenly. The luteal phase is characterized by a sustained elevation of temperature to 100 F. or more, which persists until one or two days before the next flow. There is a slight drop in temperature in the midluteal phase, corresponding to the estrogen peak. Determinations of temperature throughout the menstrual cycle have provided a simple method of determining the time of ovulation in many women.

Abnormal Bleeding in the Treatment of the Menopause.—Bleeding from the uterus may occur at any age following estrogenic therapy. This bleeding may sometimes be prolonged and excessive, particularly following large doses of estrogens, and may be particularly dangerous in women with fibroids. All women in whom estrogenic therapy is contemplated should have a careful gynecologic examination, and the presence of fibroids or carcinoma of the cervix or fundus are contraindications to its use. When estrogen-induced bleeding occurs it can usually be controlled with rest and ergonovine maleate but in occasional instances it may be necessary to perform a curettage to control it. In a few older women with fibroids the bleeding may be so prolonged and excessive that a hysterectomy is necessary.

In the treatment of the menopause an effort should be made to administer the minimum amount of estrogenic material that will control symptoms without inducing uterine bleeding. In actual practice it is not always easy to attain this ideal. Amounts of estrogen that are inadequate to control menopausal symptoms completely may induce uterine bleeding. If patients are carefully followed, those with fibroids and carcinoma of the cervix or fundus excluded, and the smallest dosage of estrogen administered that will control symptoms, treatment of the menopause is a safe and reliable procedure. Slight spotting which occurs periodically is not serious. Treatment should be discontinued until it disappears and then resumed. In most instances, when prolonged and excessive bleeding occurs with small doses of estrogenic material, it is best to discontinue treatment permanently.

Hypogonadism Before the Menopause.—Stimulation of the ovary with various gonadotropins is not very satisfactory. Chorionic gonadotropin is not nearly as effective in the female as in the male. Pituitary gonadotropin is sometimes effective in inducing menstruation in women with secondary amenorrhea and may cause ovulation in women with anovulatory cycles. In most instances substitution therapy with estrogenic material must be employed in the treatment of hypogonadism in the female. There is some difference of opinion concerning the most effective estrogen. For most purposes, estradiol in some suitable combination such as the benzoate or the dipropionate appears to be the most satisfactory product, but there are many estrogenic preparations on the market which produce excellent results. In the female, as in the male, the optimum time for the treatment of hypogonadism is the age of normal puberty. It is only by starting treatment at this age that maximum genital growth can be induced and skeletal disproportions prevented. The difficulty is that the diagnosis of hypogonadism early in puberty is much more difficult in the female than in the male because the development of the ovary cannot be determined as readily as the development of the testis. When hypogonadism is the result of a primary defect of the ovary, it is permanent and treatment is necessary during a large portion of the patient's life. The ideal form of treatment is the cyclic administration of estradiol and progesterone in a manner that simulates their normal production, so that periodic uterine bleeding is induced.

HORMONE ASSAYS

The time has arrived when the practice of endocrinology cannot be carried out adequately without proper laboratory facilities. For purposes of correct diagnosis and checks on therapy, it is necessary to have available facilities for determining the production of various hormones and the estimation of the concentration of various other substances in the blood and urine. The determination of the basal metabolism is also an essential of any adequate endocrine laboratory. It is important to be able to determine the production of follicle-stimulating hormone, androgens, estrogens, adrenal cortical steroids, etc. Facilities for determining the presence or absence of pregnancy (chorionic gonadotropin) are indispensable. It is essential to be able to make simple chemical tests—for example, determinations of sugar, sodium, potassium, calcium, phosphorus, phosphatase, total protein, albumin, globulin, nonprotein nitrogen, uric acid, creatine and creatinine—in blood and urine. Roentgen examination of the skeleton is essential in determining the effect of glandular abnormalities on growth. Gynecologic examination, endometrial biopsies and examination of the vaginal smear may furnish important information.

RELATION OF HORMONES TO CARCINOMA

Carcinoma of the Prostate.—A few years ago Huggins [10] reported that orchiectomy sometimes produced striking improvement in patients with carcinoma of the prostate. Metastases in bone sometimes disappeared after this procedure, on the basis of roentgen examination. Huggins originally reported the results of orchiectomy in 20 patients with advanced carcinoma of the prostate. All had demonstrable metastases or local infiltration beyond the prostatic capsule. In 2 patients there was no obvious improvement from the operation. In the remainder clinical improvement was obtained for varying periods postoperatively. Eleven patients died during the first two years after orchiectomy and 4 others died within thirty-six to sixty-three months. Two deaths were the result of intercurrent infection. The median survival time for the 15 fatal

10. Huggins, C.: Prostatic Cancer Treated by Orchiectomy: Five Year Results, J. A. M. A. **131**:576-581 (June 15) 1946.

cases was sixteen months, with improvement during eleven months of this period. Five patients survived more than five years after orchiectomy. Of these, 4 showed no signs of disease and 1, although apparently well, had a tumor mass in the region of the seminal vesicles. It would be premature to suggest that actual cure of the disease has been achieved in any case. Huggins and Scott [11] have recently reported the effects of bilateral adrenalectomy in 4 men with rapidly growing metastatic carcinoma of the prostate after orchiectomy had failed to arrest the malignant growth. Two men survived only thirty-six and fifty-four hours after complete adrenalectomy. The third patient lived eleven days and the fourth patient one hundred and sixteen days. Adrenalectomy did not appear to prolong life in these patients. The urinary 17-ketosteroids fell to a level of less than 2 mg. per day. This observation furnishes the first direct proof that the chief sources of urinary 17-ketosteroids are actually the gonads and the adrenals. The advance of the malignant process in a man with low androgenic activity suggests a factor apart from the stimulating effect of testicular and adrenal androgens. To this factor Huggins has given the name "androgen independence." Huggins has expressed the opinion that androgen may be necessary for the development of carcinoma of the prostate but that once the process is set in motion it may continue without androgenic stimulation.

Reports are appearing from various clinics on the effect of surgical castration and functional castration with estrogens in patients with carcinoma of the prostate. All observers are agreed that striking initial improvement is produced in most of the patients and most observers feel that life is prolonged. Many patients have died of carcinoma of the prostate after initial improvement. Sufficient time has not yet elapsed to determine whether castration ever produces a permanent cure. It is Huggins' opinion that bilateral orchiectomy is a more effective procedure than the administration of diethylstilbestrol.

Carcinoma of the Breast.—For years it has been known that occasionally in women with carcinoma of the breast removal of both ovaries produces some improvement. Adair and others [12] have recently reported that functional castration of women by the use of testosterone propionate in oil often produces striking clinical improvement. This improvement may consist in a decided reduction in the size of the local lesion in the breast, a decrease in the size of the metastases in the neighboring structures and an improvement in the metastatic lesion in bone.

The results are by no means as striking as those of castration in carcinoma of the prostate. It is the impression of some workers in this field that testosterone propionate is primarily of value when bony metastases are present. For reasons which are not clear at the present time, after the age of the menopause estrogens are said to produce some improvement in soft tissue metastases, whereas before the menopause they are supposed to aggravate the condition. As time has gone on, most patients have died of carcinoma of the breast. Results, while interesting, are not nearly as conclusive as those in carcinoma of the prostate.

Carcinoma of the breast may be produced by administration of estrogen in certain mice, but, up to the present time, there is no evidence that the administration of estrogenic material causes carcinoma of the breast in women. Many women have been frightened through articles appearing in the lay press implying that use of estrogenic material in the treatment of the menopause is harmful and likely to produce carcinoma of the breast. It is significant that among the large numbers of women receiving estrogens for treatment of the menopause, carcinoma of the breast is rarely noted. The danger of development of cancer of the breast can therefore scarcely be used as an argument against the treatment of the menopause with estrogen.

THE PANCREAS

No important development has recently taken place in knowledge of the internal secretion of the pancreas. The use of various insulins has been perfected and gradually more is being learned about islet cell tumors of the pancreas which produce hypoglycemia.

One interesting observation has been that by Dixon and others [13] at the Mayo Clinic and by Ricketts, Brunschwig and Knowlton [14] at the University of Chicago on the effect of total pancreatectomy in a patient with diabetes mellitus. They noted that the total insulin requirement was unaffected by this operation.

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ABSTRACT OF DISCUSSION

TREATMENT OF THE MENOPAUSE

QUESTION: What is the most satisfactory endocrinologic treatment of the menopause?

ANSWER: About 40 per cent of women have no untoward symptoms following cessation of menstruation. These women require no treatment. The remaining 60 per cent have symptoms which vary in intensity from patient to patient. In some women the symptoms are severe and include frequent hot flushes, palpitation, nervousness and various psychic disturbances such as persistent depression and paranoia. The duration of the symptoms varies from a few months to many years and the duration of treatmen. varies accordingly. The best method of treatment is to give the minimum amount of estrogenic material that will control symptoms. There are a variety of synthetic and natural estrogens available for this purpose. Of the synthetic estrogens, diethylstilbestrol has been used most widely. The minimum dose that will control symptoms completely varies from 0.25 mg. to 1.5 mg. daily. Most women do not require more than 0.5 mg. daily. In these doses diethylstilbestrol rarely produces toxic effects, although various claims of superiority have been put forth for other estrogens, such as dienestrol. The synthetic estrogens possess the advantage of being very effective by mouth. Of the natural estrogens the most effective probably is estradiol. It is usually given in the form of the benzoate or the dipropionate and is more effective when administered intramuscularly than when given by mouth. The minimum dose required to control symptoms varies from 1.67 mg. every two weeks to 5 mg. twice a week. It is important to carry out a careful pelvic examination before instituting estrogenic therapy for the menopause. This form of treatment is contraindicated in women with carcinoma of the cervix and in most patients with uterine fibroids. In women with fibroids excessive bleeding may start, either during estrogenic therapy or after its withdrawal. Even in women whose uterus appears to be normal prolonged and excessive

11. Huggins, C., and Scott, W. W.: Bilateral Adrenalectomy in Prostatic cancer: Clinical Features and Urinary Excretion of 17-Ketosteroids and Estrogen, Ann. Surg. **122**:1031-1041 (Dec.) 1945.

12. Adair, F. E., and Hermann, J. B.: Use of Testosterone Propionate in Treatment of Advanced Carcinoma of the Breast, Ann. Surg. **123**: 1023-1035 (June) 1946.

13. Dixon, C. F.; Comfort, M. W.; Lichtman, A. L., and Benson, R. E.: Total Pancreatectomy for Carcinoma of the Pancreas in a Diabetic Person, Arch. Surg. **52**:619-639 (June) 1946.

14. Ricketts, H. T.; Brunschwig, A., and Knowlton, K.: Effects of Total Pancreatectomy in Patient with Diabetes, Am. J. Med. **1**: 229-245 (Sept.) 1946.

bleeding may follow the prolonged administration of estrogen in large doses. Treatment should be interrupted every three or four months to determine whether it is still necessary and the patient should be followed carefully during treatment. It is probably best not to administer estrogen to any woman in whom the presence of carcinoma of the breast is suspected although it has been claimed that in women after the age of the menopause estrogenic therapy may be of some value in reducing the size of soft tissue metastases.

TREATMENT OF OBESITY

QUESTION: Are endocrine products useful in the treatment of obesity?

ANSWER: Obesity may or may not be associated with endocrine deficiencies although the presence of hypogonadism in patients with obesity is common. Desiccated thyroid may be employed in moderate doses (2 to 4 grains [0.12 to 0.25 Gm.] daily) under careful supervision to supplement a weight-reducing diet. Patients must be followed carefully during the administration of this material because in some instances symptoms of intoxication develop with small doses. Great care must be taken to avoid self medication with thyroid products. In adolescent boys suffering from the Fröhlich syndrome the administration of chorionic gonadotropin may produce a complete transformation without a weight-reducing diet. As a result of the stimulation of the production of the male sex hormone the muscles develop, shoulders become broader, hips narrower, and breasts and abdomen smaller. If the obesity associated with this condition is severe, it is necessary to supplement the administration of chorionic gonadotropin with the administration of a weight-reducing diet.

EXTRACTS OF ADRENAL CORTEX

QUESTION: For what conditions are extracts of adrenal cortical substances effective?

ANSWER: The most important indication for the use of adrenal cortex extract is the presence of Addison's disease. It is the only material that is effective in the treatment of a crisis of this disorder, whereas for maintenance therapy the synthetic material desoxycorticosterone acetate is preferred because of its low cost and the fact that it may be implanted subcutaneously in the form of pellets, thereby eliminating the necessity of daily injections. There are many reasons for believing that the cortex of the adrenal gland produces a material which plays an important role in the resistance of the body to trauma and infection. Administration of adrenal cortex extract has accordingly been tried in the treatment of shock, in the treatment of severe infections to supplement specific substances and in the treatment of patients who have severe reactions following surgical procedures. There are data which suggest that adrenal cortex extract is of some value in the treatment of these conditions. The cost of the material and its rather limited supply have prevented its adequate trial in conditions which have just been mentioned. In some instances the doses used have been too small to produce much improvement. In the presence of shock and overwhelming infection it is probably necessary to give the material in doses of not less than 10 cc. per hour.

RADIOACTIVE IODINE

QUESTION (Dr. Fred Kauffmann, Canton, Ohio): In what way can radioactive iodine be handled for practical purposes?

ANSWER: Radioactive iodine is not yet ready for routine clinical use. To treat patients with toxic goiter satisfactorily with this material there must be an adequate setup for measuring the dose administered and the amount of material taken up by the thyroid gland and the rate at which it disappears. The equipment necessary for this purpose is relatively expensive and its application requires specially trained personnel. Radioactive iodine has therefore been used in only a few clinics up to the present time. All radioactive material has to be handled with the greatest care because of serious consequences which may follow overexposure to the powerful rays emitted.

ABSTRACT OF DISCUSSION

The answers to the following questions were by Dr. Chester S. Keefer, Boston, whose original presentation comprised a lantern demonstration and was therefore not suitable for publication.

PENICILLIN BLOOD LEVELS

QUESTION (Dr. L. H. Hirsh, Milwaukee): What is the relation of blood levels to tissue levels in use of penicillin?

ANSWER: Penicillin diffuses into red blood cells in about 10 per cent of the concentration of that in the plasma. Very small amounts diffuse into the cerebrospinal fluid, even after large intramuscular or intravenous injections of penicillin. Penicillin can be found in pericardial, peritoneal, pleural, joint and edema fluid. The concentration in general is lower than that found in the blood at the same time. Little, if any, diffuses into the tears or saliva, or the pancreatic juice or the milk. It passes through the placenta from mother to infant. The amount present in placental cord blood is approximately 40 per cent of that found in maternal serum. It has also been ascertained that penicillin diffuses into the kidney, small intestine, lung, buccal mucosa, bile, skin, liver, adrenal glands, pancreas, heart, voluntary muscle and spleen. Practically none is found in the brain and bone marrow, even one hour after intravenous injection of fairly large doses. The dura mater, cornea, lens and vitreous humor contain no penicillin, and nerve tissue only traces. In brief, penicillin diffuses into various organs of the body in much lower concentration than that found in the plasma.

PENICILLINASE

QUESTION (Dr. A. C. Worley, Fort Wayne, Ind.): Do body cells develop penicillinase? If so, how long does resistance last?

ANSWER: There is no evidence that the body cells develop penicillinase. Penicillin is not inactiviated by any of the body fluids, pus or necrotic tissue. Some bacteria, notably the Staphylococcus and the gram-negative bacilli, may produce penicillinase.

MIXTURES OF ANTIBIOTICS

QUESTION: Can streptomycin and penicillin be mixed in the same syringe?

ANSWER: Yes, there is no contraindication to mixing the two together for simultaneous injection.

BACITRACIN

QUESTION: Are there any new effective antibiotics?

ANSWER: The only new antibiotic that has been investigated on a limited scale is bacitracin. Dr. Meleney and his associates have used bacitracin locally for the treatment of infected wounds. It has the same general scope, as far as bacteria are concerned, as penicillin.

TREATMENT OF ORDINARY SORE THROAT

QUESTION: Do you think it advisable to treat ordinary sore throat with penicillin and/or sulfonamide drugs?

ANSWER: Yes. Most instances of sore throat are due to hemolytic streptococcus infection. Penicillin and/or the sulfonamide drugs can prevent suppurative complications and reduce the total number of days of illness.

STREPTOMYCIN NOT INFECTIOUS

QUESTION (Dr. Erling S. Wedding, Brooklyn): Have any strains of streptomycin ever been demonstrated to be pathogenic to man or experimental animals?

ANSWER: I do not know of any cases in which Streptomyces griseus has been responsible for infection in man.

ABSCESS OF THE LUNG

QUESTION (Dr. William Klein, New Brunswick, N. J.): Have you found a greater incidence of pulmonary abscesses following the use of penicillin in pneumonias?

ANSWER: From a study of the large number of cases reported to the Committee on Chemotherapeutic and Other

Agents of the National Research Council, there is no evidence that the use of penicillin in the treatment of pneumonias is followed by a larger number of pulmonary abscesses.

ORAL PENICILLIN

QUESTION (Dr. Charles P. Ryland, Washington, D. C.): Please discuss the efficacy of penicillin orally.

ANSWER: At least three to five times as much penicillin should be given by mouth as is given parenterally. It has been found to be extremely effective in the treatment of pneumococcus pneumonia, gonococcic urethritis, hemolytic Streptococcus infections of the throat and pharynx, and other mild or moderately severe infections that respond to penicillin.

STREPTOMYCIN TIME-DOSE RELATIONSHIP

QUESTION (Dr. Belle Jacobson, New Rochelle, N. Y.): Is it necessary to give streptomycin every three hours in the treatment of tuberculous meningitis?

ANSWER: There is not enough information available concerning time-dose relationships to make any precise statement concerning the time interval between the injections of streptomycin in the treatment of tuberculous meningitis. It is not unlikely that injections every six hours throughout the day will be adequate, for the reason that streptomycin is excreted by the kidney much more slowly than is penicillin.

UNDULANT FEVER

QUESTION (Dr. P. Blair Ellsworth, Idaho Falls, Idaho): What is the latest treatment for undulant fever?

ANSWER: The best results that have been reported in the treatment of undulant fever, particularly the early cases—that is to say, patients who have been ill for less than two weeks—have been from the combination of sulfadiazine and streptomycin. Streptomycin should be continued for at least four weeks in amounts of at least 2 Gm. a day; sulfadiazine should be continued for a similar period of time, depending on the reaction of the patient. In the chronic cases of undulant fever, the evidence is far from convincing that any of the chemotherapeutic agents are responsible in shortening the course of the disease.

INTRASPINAL INJECTIONS

QUESTION (Dr. George Vryonis, Alexandria, La.): What dilutions of penicillin and streptomycin should be used in intraspinal injections? What undesirable results may follow?

ANSWER: Penicillin should be diluted so that not more than 1,000 to 2,000 units per cubic centimeter of isotonic solution of sodium chloride are used. The maximum dose should be not more than 25,000 to 50,000 units in a twenty-four hour period. For streptomycin, the maximum dose in a twenty-four hour period should be 50 to 100 mg., diluted in 10 to 20 cc. of isotonic solution of sodium chloride. With low dilutions and a volume of solution that is equal to that which has been withdrawn after lumbar puncture, there are usually no undesirable effects. If on the other hand, one uses high concentrations and small amounts, headaches, meningismus and, rarely, convulsions may follow.

PERTUSSIS

QUESTION (Dr. Benjamin Feldstein, New York): Is streptomycin of value in the treatment of pertussis?

ANSWER: So few patients with pertussis have been treated with streptomycin that it is impossible to answer this question with certainty. A few patients with pertussis associated with pneumonia and fever have been treated with streptomycin with striking results. There are several studies under way at present, so that more information concerning the value of streptomycin in pertussis will be forthcoming.

COMBINED INJECTIONS

QUESTION (Dr. H. H. Schuman, Springfield, Mass.): Is there any contraindication to using both penicillin and streptomycin in a single combined injection?

ANSWER: There is no contraindication to using both substances in a single combined injection. They should both be made up freshly before injection.

TOLERANCE TO PENICILLIN

QUESTION (Dr. A. I. Rosenblum, Chicago): What is the present status regarding the development of tolerance to penicillin following repeated uses for different diseases?

ANSWER: There is no evidence that the use of penicillin repeatedly builds up a tolerance on the part of the patient to its effective use when infections occur.

DISTILLED WATER OR SALINE SOLUTION

QUESTION (Dr. L. C. MOERIS, Chicago): Is it desirable to administer streptomycin in distilled water rather than in saline solution?

ANSWER: Streptomycin may be administered either in distilled water or in saline solution. There is some evidence that mixing streptomycin with isotonic solution of sodium chloride decreases its activity. This has been demonstrated in vitro, but so far there is no evidence that using streptomycin in saline solution for the treatment of infections in man has decreased its potency.

PROPHYLAXIS OF RHEUMATIC FEVER

QUESTION (Dr. J. L. Hrdina, Cicero, Ill.): Do you recommend the daily oral use of penicillin in the prophylaxis of rheumatic fever for long periods, say two to four years' continuous use?

ANSWER: No one has had any experience with the daily oral use of penicillin for two to four years continuously. There is some evidence, based on experience over the last two years, that penicillin given in amounts of 50,000 units twice daily will prevent Streptococcus sore throat when patients are under carefully controlled conditions. In this way the incidence of the recurrence of rheumatic fever may be reduced.

LEGAL LIABILITY

QUESTION: What legal liability can a physician incur at this time, knowing the possible permanent disabilities the patient will incur with the use of streptomycin?

ANSWER: I do not know. This is a matter that should be taken up with legal counsel in order to get a specific opinion.

ALLERGIC REACTIONS

QUESTION: I suggest a plea for more accurate reports on the allergic reactions following the injection of penicillin in wax and peanut oil. The incidence seems higher than 5 per cent and the distress to patient and physician much higher than 50 per cent. Can a different menstruum be made?

ANSWER: No menstruum has been developed other than peanut oil and white wax for adequately delaying the absorption of penicillin from local deposits. In a controlled series of cases studied by Dr. Harry Dowling in Washington, D. C., the incidence of allergic reactions following the injection of penicillin in oil and wax was 5 per cent. This is a personal communication from the investigator.

ANTIBIOTICS AND THE COMMON COLD

QUESTION: Is it worth while to give antibiotics in the treatment of the common cold or influenza?

ANSWER: There is no evidence that any of the antibiotics influence the course of influenza or the common cold.

A Vaccination Record.—In less than a month more than 6,370,000 people were vaccinated in New York City, over 5,000,000 of them within the two week period following the appeal for universal vaccination made by the Mayor. Never before had so many people in one city been vaccinated in such a short time and on such short notice. Thanks are due to the press and radio for giving so generously of their space and time to bring necessary information to the public. Had it not been for them and for the intelligent cooperation of the public and the generosity of private physicians and volunteer workers, notably from the American Red Cross and the American Women's Voluntary Services and former Air Raid Warden groups, it would have been impossible to have achieved this remarkable record.—Weinstein, Israel, M.D., An Outbreak of Smallpox in New York City, *American Journal of Public Health*, November, 1947.

Special Article

FOODS FOR EMERGENCIES

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"Our difficulties will be greatly lessened if we have a long-range food policy which will ensure that during the war and the postwar period, however poor the nation or part of the nation may be, every family will be assured of sufficient food to maintain them in health."—Sir John Orr and David Lubbock, Feeding the People in War Time, London, Macmillan & Co., Ltd., 1940.

Writing in 1942 on the subject "Unusual Foods of High Nutritive Value," we urged reevaluation of supplies of food, with emphasis on a number of resources which theretofore had not been tapped extensively and which warranted more consideration in developing plans for feeding populations for which supplies of food were limited. The undernutrition of hundreds of millions of the European population precipitated by the war and scarcely arrested, if at all, since the ending of hostilities, prompts reiteration of this subject. Also a number of the foods which we considered in our previous paper have assumed immense importance in many of the war-torn countries, and some account of this experience is now available for review.

Two general observations relate to this experience; each of them has been repeatedly affirmed. The first is that starvation in the European countries, bad as it has been, has everywhere been less than was anticipated from estimates of food supplies available. The second is that deficiencies of specific nutrients and especially deficiencies of vitamins have been relatively inconspicuous. The reasons include the fact that persons who are undernourished compensate to some extent by curtailing their activities. Children are less active in their play, and the work output of adults falls unconsciously. The growth of children is retarded. Likewise with subnutrition goes depression of basal energy exchange; in starvation the basal metabolic rate may be as low as minus 40, which represents a physiologic adjustment. The need for calories is restricted by these means, and loss of weight lags behind what would be expected were judgment limited to knowledge of the calories available. Also in consequence of diminished expenditure of energy the requirement for several nutrients is lessened and the appearance of signs of gross deficiency, either of vitamins or protein, is postponed. However, there is yet another reason for discrepancies between the loss of body weight anticipated and that observed. This, namely, has been the ability of starving populations to supplement their diets with edibles which are not included in customary estimates of food supplies. Thus some extra calories are obtained, and in addition, as a rule, the unusual foods consumed are often good or even excellent sources of minerals and vitamins. Thereby the diet as a whole in many European countries, although inadequate with respect to calories and providing much less animal protein and less fat than is desirable, has been relatively improved in certain instances with respect to minerals and vitamins. Exceptions have been noted. In Spain, where for many people the staple foods were white bread and polished rice, the number of cases of mental and nervous disorders attributed to deficiency of B vitamins is reported to have increased greatly, in contrast to experience in Leningrad and Stalingrad, where hundreds of thousands died of starvation, but vitamin deficiency was not apparent.

We made comment in our previous paper that the diets of primitive populations, with food selection limited to unsophisticated foods, compared most favorably with the diets of those nations which are most advanced in general culture and whose people have certain silly notions about what is fit for food. Primitive man was constantly in danger of starvation from inadequate supplies of food, but the foods which he obtained from his natural environment were relatively rich in vitamins, in minerals and in protein. A happy custom of primitive man was to eat the entire carcass of his kill, including the intestine, which with the organ meats, notably the liver, was rich in vitamins. He ate these morsels first by preference, he drank the animal's blood, he was none too squeamish in his taste for fish, but took whatever he could catch and ate it whole. Snakes and rodents were delicacies, and insects, termites and the like, all rich in nutrients of the highest value, were quite acceptable. Wild fruits and vegetables were consumed either fresh as found or after a minimal period of storage. Later, with the development of agriculture, the cereal grains came into use, but so long as milling methods remained primitive these provided much more nutrient material than is obtainable from the highly processed cereals of modern mills.

The inhabitants of the European countries overrun by Germany reverted so far as they were able to the food ways of primitive people. Many products which in normal times were not considered fit for human use have been found acceptable in this time of need. The wheat and other grains available were ground whole for human use or milled to high rates of extraction, whereby, for example, from 100 parts of wheat from 85 to 100 parts of flour are produced, as compared to the 65 to 72 parts of flour yielded as white flour by the modern flour mill. No skim milk was allowed to go to waste, and the whey obtained from making cheese was utilized for food. Organ meats were cherished and in places even the blood of slaughterhouse animals was consumed. The populations of Europe were handicapped in this reversion to more primitive food ways by ingrained habits, by taboos, by lack of ingenuity and by numbers. The natural food environment of Europe may have provided enough in primitive times, but it falls far short of being ample for a population like that of modern Europe. Nevertheless, something could be done to eke out meager rations, and what was obtained by these and other means helped to alleviate the worst effects of famine.

"The bread is dark and soggy, made of several kinds of coarse grain," reads one report. Other than the rationed foods, and they provided only 1,500 calories daily, people could "buy" sea gulls, crows and strange fish which formerly were considered unfit for human consumption. Meat had disappeared, even horse meat. The women and children scoured the fields and roadsides for edible plants. The forests were finecombed for mushrooms and berries. Dandelions, nettles, acorns, leaves and nuts all had their uses. Every little plot of ground, even every window box, became a victory garden. That was in Norway. In Holland, tulip bulbs

Because of lack of space the section on Milk and that on Fats have been condensed for publication in THE JOURNAL, and the bibliography has been omitted. The complete article appears in the authors' reprints.

and sugar beets were consumed as food. Both caused diarrhea when taken in large amount. Rhubarb leaves proved toxic. The same was true of beechnuts. Thus at times more harm than good resulted from the practice of foraging. In Germany, in the spring of 1947, when coarse bread was made from high extraction flour, this bread and potatoes were the foods principally responsible for a nutritional situation which otherwise would have been more serious than should have been expected from the ration. The diet largely consisted of bread and potatoes with a few beans and peas, a bit of cheese and a few onions. The fat allowance was 9 Gm. a day for adults. The weekly meat allowance was usually consumed at one meal.

EDIBLE WILD PLANTS

Weeds and other plants have been used as food by every famished population. The varieties available in Belgium were described by Hermans. The Russians resorted to cooking inedible greens to make a paste rich in carotene. This was eaten as a spread on bread. Sources of vitamin C were short in many countries. In England as well as on the Continent rose hips were collected and reduced to syrup or jelly. Pomegranate boiled and concentrated was used in Russia. Germinating grains have long been known to be a source of ascorbic acid. United States soldiers in the Pacific area were given a manual issued by the War Department which illustrated and described both edible and poisonous plants. It was intended as a guide for soldiers separated from their units and dependent on foraging for their survival. The manual covered all Polynesia, Micronesia, Melanesia, the Malay Peninsula and the Philippines. For practical purposes it also covered Indo-China, Thailand, Burma and Eastern Asia. An astonishing number of herbs, ferns, palms, grasses, tuber seeds and fruits were described as being edible and nutritious.

Issued in 1943 by the Office of War Information of the United States government was a list of edible weeds with directions for their preparation. Mentioned were dandelion, lamb's quarters, plantain, poke, purslane, wild chickory and dock. Some of these are to be found in every vacant lot and on other neglected ground. Others grow abundantly along roadsides and hedges or by streams and in the woods. A leaflet containing similar information was distributed by the New York Department of Health. Mentioned in it were milkweed, stinging nettle, summer mustard and sorrel. Mentioned also in a reference was a book entitled "Weeds" by W. C. Muenscher.

Among the edibles in nature which in emergencies can serve as food is the acorn, which held a place of importance in the diet of the American aborigine. After parching over coals the meat is sweet and palatable. It may be powdered to make a flour. Many wild plants served the Indians and early settlers of America. Among those noted by Carr are the tuberous roots of the catbrier or greenbrier (Smilax), the roots of the common cattail, the bulb of the sego lily and persimmons and poke weed.

KITCHEN GARDENS

The kitchen garden has made an important contribution through these recent years of shortages of food in Europe, and gardens in America have helped to supplement the diet here and thus to release less perishable foods for export. Greater savings of food for export can be made by avoidance of waste, not only waste of food itself but loss of the nutrients in foods during their handling and preparation in the kitchen. Efforts to teach this lesson during the war were not without effect. The problem is of supreme importance but not a part of the subject of this paper. By its national gardening program the Department of Agriculture is encouraging the continuation of the wartime garden program. City planners are encouraged to provide small garden plots for use by urban dwellers. Not only is the contribution of fresh food from the garden of the greatest value in nutrition, because fresh foods contain vitamins some part of which is lost when the foods are shipped to distant markets, but from the gourmet's point of view fresh foods contribute greatly to the attractiveness of the meal. No tomato tastes as good as one just picked, no lettuce, no sweet corn, no peas or green beans, no strawberries or melons can compare with those grown in one's own garden. Also the variety of food that can be made available is much greater than can be found in local markets. Millions of city and suburban dwellers with no previous experience became skilful gardeners in the war years and learned that gardens pay in increased health and satisfaction. Also many persons for the first time in their lives learned to eat these wholesome foods.

In England in the war the Ministry of Food allotted land from parks and other open spaces and provided blueprints for the gardens. The allotments were "10 perches" in size, a plot of about 300 square yards, say 30 by 90 feet (9.1 by 27.4 meters). A study of ninety-eight of these allotments showed an average production in one year of 411 pounds (186.4 Kg.) of potatoes and 1,088 pounds (493.5 Kg.) of other vegetables. The plan involved successive plantings, so that in the English climate it was possible to obtain a fairly even supply of products over the year. The amount was sufficient to meet the requirements for vitamins C and A for a family of five and to add importantly to the supply of other nutrients and calories.

POTATOES

Of all the vegetables, however, the one which aided most in the support of human life in war-torn Europe was the white or Irish potato. The Ministry of Foods in England guaranteed the growers a price for all surplus potatoes. Their distribution was well controlled and they contributed to the calories of the diet even more importantly than wheat. Drummond called bread and potatoes "buffer energy foods" because at the height of rationing in the United Kingdom they remained in adequate supply, unrationed, to serve as buffers for diets which otherwise would have been too low in calories.

The potato thus is properly regarded as a food of great value in emergencies. Unfortunately, the crop is not entirely dependable, and when great reliance has been placed on it failure of the crop has resulted in widespread famine. Another problem with potatoes is the high water content and thus the cost of transportation. This has limited the usefulness of potatoes for relief feeding abroad. The ocean freight alone is enough greater than that of flour so that flour at a cost of 6 cents a pound (13.2 cents a kilogram) has been less expensive than potatoes delivered free of charge to United States ports. Potatoes, furthermore, are sensitive to freezing. Great losses occurred in storage in Europe in the cold weather of 1942-1943.

For the several reasons mentioned it would seem to be desirable to provide for large scale processing of potato crops. Dehydration is a possibility, but is relatively expensive. Potato flour can be made rather inexpensively and has been reported as selling in a competitive market at only 8 cents a pound (17.6 cents a kilogram) which puts it in a class with wheat flour. Uses for potato flour should be thoroughly explored. Its admixture with wheat flour in making bread is a long-established practice, although little used since World War I. Many other uses could be found. Potatoes when properly prepared for eating make important contributions to the ascorbic acid content of the diet. Potato flour probably contains no ascorbic acid, but this difficulty could readily be corrected by suitable fortification. The nicotinic acid and thiamine of potatoes are presumably retained in processing to flour. Only about 40 per cent of the nitrogenous substance of potato is protein. The balance consists of amides, amino acids and purines; yet the biologic value in nutrition, although less than that of casein, is said to be superior to that of the combined nitrogenous substance of wheat, of which 90 per cent consists of protein. The principal protein in potato (tuberin) is not superior in value to the proteins of wheat, from which Chick and Cutting have concluded that some portion of the non-protein nitrogenous material must be utilized as protein.

PROTEIN RESOURCES

Shortage of protein of good biologic quality has been serious in many parts of Europe as well as in the Far East.

Blood.—In the winter of 1944-1945 plasma obtained from slaughterhouse blood played a part in Amsterdam in the treatment of famine edema. A pediatrician was the first to call for it. He wanted it for children in the 6 to 14 year age group, in which the mortality rate had risen rapidly from the time that supplies of rationed milk had been suspended. Two butchers were placed under supervision for the preparation of this plasma. Soon thereafter general practitioners began to use the product for patients with hunger edema. Benefit was observed with as little as 500 cc. per week. The fact that a dose of 6 Gm. of animal protein a day, which was all that this provided, was lifesaving led to the conclusion that lack of certain essential amino acids in the almost entirely vegetable diet had been responsible for the edema and for increased mortalities. The demand for the plasma increased so much that all slaughterhouse blood was used for this purpose. It was fed at first cooked in pancakes, later as bouillon or in brown bean soup. Whole blood, incorporated in sausage (Blutwurst), which had been consumed before in parts of Europe, was not acceptable in Amsterdam. Physicians, however, prescribed it for anemia. In Russia and in parts of Germany, whole blood was used in bread. In Switzerland, a mixture of potato and blood was recommended.

Fish.—The normal catch of fish by European fishermen was seriously diminished while war lasted, owing mainly to confiscation of trawlers and other fishing boats for wartime purposes. Fishing now is being stimulated by every means available in order to increase the supplies of protein. Unfortunately, only a relatively small proportion of the normal catch of fish is at present utilized for food. The balance is diverted to fishmeal fertilizer or is thrown away. The protein of this waste was separated by Deuel for study of its biologic activity. It equaled casein in potency for regenerating plasma protein in animals made hypoproteinemic by exsanguination.

In addition to their value as a source of protein, small fish offer the advantage of containing edible bones, thus serving as a source of calcium. A report from India by Basu and his associates contained the account of a study of calcium balance made on human subjects who were given small whole fish as the only source of calcium. A daily intake of 70 Gm. maintained a positive balance. Calcium deficiency is prevalent in the rice eaters of Bengal and other parts of India where milk is not obtainable, and an active interest in this matter is apparent from numerous studies reported in the scientific literature of India. Aykroyd, in a consideration of Indian diets, pointed to the fact that India of necessity must be self contained as regards food supply and that the existing relation between population and the land necessitates a national diet composed of foods giving a high calorie return for each unit of the land. Attempts to increase the production of foods not falling within this category, foods such as milk or meat, present great difficulties. Adolph, writing on conditions in China before the war, made the comment that vegetarian people are usually vegetarian not because of dietetic whims but for economic reasons. The equilibrium between food supply and population is so delicate that disturbance of the status quo may be at once reflected either in emigration or in a mounting death rate from starvation. Cereals and legumes provide some 88 per cent of the calories consumed in China. This type of situation seems to us to call for great expansion of the fisheries, with due attention paid to Deuel's suggestion for more economy in the utilization of the catch. It can be maintained that an increase of the food supply in the Orient would only lead to further increase of the population. Our suggestion here, however, is not so much an increase of the total calories, but rather an improvement in the quality of the diet.

The amount of animal protein obtainable from the sea is almost limitless. Areas in which life is of unusual abundance are the North Sea, the Norwegian Sea, the waters around Newfoundland and off many of the coasts of all the continents. The yield of coastal waters can be increased by fertilizing. This was shown, for instance, by an experiment in Scotland. An inland lock or bay of salt water with an area of about eighteen acres and an average depth of 2 meters was fertilized with so little as 600 pounds (272.2 Kg.) of sodium nitrate and 400 pounds (181.4 Kg.) of superphosphate. A neighboring lock received no fertilizer. There was an immediate rise in the vegetation of the fertilized lock to three to four times the original amount and the growth of fish leaped upward. Baby flounders grew in thirteen months to a size equal to that of two or three years' growth in the North Sea, itself a rich feeding ground.

We mentioned in our earlier paper the carp culture of German inland lakes. The fish farms of Central Europe produce as much as 500 pounds (226.8 Kg.) of fish per acre, which has been compared to the 200 pounds (90.7 Kg.) of beef or mutton obtainable from pasture land of quality. A bulletin of the Department of Agriculture explains how to manage farm fishponds for food production.

Soy Beans, Peanuts, Wheat Germ and Corn Germ.—Protein of relatively high biologic value is provided by beans and peas. Early in the emergency created by the war, production goals for soy beans were raised for

two important purposes, (1) for the oil to replace the diminishing supply of fat and (2) as a source of protein. The protein of soy beans is excellent with respect to all of the essential amino acids except cystine. The same, indeed, is true of common beans. But since wheat flour contains cystine, the use of beans with bread, or better still of baked beans and brown bread, provides a source of protein which is adequate. The vitamin values of the soy bean compare favorably with those of meat; the choline content is higher than that in leafy vegetable roots and grains. In the war soy bean flour that was free of fat found a ready outlet for some purposes, notably in doughnut manufacture. Its widespread household use, however, lagged far behind what had been desired. Milk made from soy beans has proved its usefulness especially for the feeding of children and invalids in regions of the world, especially in China, Thailand and India, where other milk is unavailable. A cookbook devoted entirely to the soy bean contains precise directions and a large group of recipes for using both the garden type of soy bean and the flour prepared from field beans.

The peanut crop was also much expanded in the war years. In this instance consumer acceptance was more satisfactory. Sherman has pointed out that beans, peas, peanuts and soy beans could assume a considerably larger part in the human diet with nutritional as well as agricultural advantage.

Wheat germ and corn germ customarily diverted to animal feeding by the millers of flour and degerminated corn meal represent a source of protein of high biologic quality that is of more importance than has been assumed. It is estimated that some 150,000,000 pounds (68,038,800 Kg.) of wheat germ and 600,000,000 pounds (272,155,000 Kg.) of corn germ might be made available for human consumption in this country. The total amount has been compared to the 500,000,000 pounds (226,796,000 Kg.) of skim milk powder produced in 1941.

Another source not only of a protein reputedly excellent in biologic quality but also of fat is the sunflower seed. The nutritive value of sunflower seed has long been recognized, especially in Russia, where great quantities are consumed. Sunflower grows in almost any soil and its cultivation might be increased with advantage in many countries.

Yeast.—An almost limitless potential source of protein of relatively high nutritive value is yeast. Mention was made of yeast in our earlier paper, but more information is now available because extensive effort was directed toward its development in the war years. Production of yeast for food was undertaken in this country, in Germany, in England, in Jamaica and in Puerto Rico. Food yeast was grown under primitive conditions and used apparently with great advantage in an internment camp in Java. Yeast requires sugar for its growth, likewise a source of nitrogen. For the latter, ammonia will suffice. In the camp in Java, a diastase was obtained by growing mold on corn and with this diastase sugar was produced from starch wastes such as old inedible potatoes. For the source of nitrogen, spoiled fish and spoiled meat were used, and when the amounts of these proved insufficient, ammonia was distilled from urine. The weekly yield of food yeast amounted to more than 60 Kg., an amount significant as a supplement to the meager diet provided by the Japanese. In Puerto Rico, surplus molasses was the culture medium, with urea obtained from sewage supplying the nitrogen. In Germany, yeast was cultured on wood sugar in amounts said to have exceeded 100,000 tons a year.

The protein of yeast has been found to be deficient in the sulfur-containing amino acids methionine and cystine; however, methionine may not be required by man if his diet contains cystine. Cystine is contained in the protein of rice or wheat, and either rice or wheat flour usually constitutes a large part of the diets of people obtaining little animal protein. Deficiency of yeast in sulfur-containing amino acids, therefore, may not represent a serious disadvantage to the use of yeast. The studies in Puerto Rico supported the opinion that the protein of food yeast (Torula) is lower in biologic value and hence lower in net protein value than that of dried brewers' yeast, and yet as good as that of soy flour and much superior to that of navy beans, rolled oats, whole wheat flour and whole corn. A purified yeast protein obtained in Germany by treatment of yeast with alkali and subsequent precipitation with acid alcohol was found effective in maintaining nitrogen balance in experiments on man, white rats and hogs.

Approximately 10 per cent of the total nitrogen of yeast is nonprotein nitrogen, a relatively large part of which is present in the form of purines, and the effect of this when yeast is used in human nutrition appears not as yet to have been fully explored. Large daily doses (130 Gm.) increased the concentration of uric acid in the blood and urine. On the other hand, relatively smaller amounts did not have these effects. An amount of yeast as small as 10 Gm. daily, to judge from studies made by Sure with rats, may be of value as a supplement to the proteins of white flour or white rice. It is possible that further experiments will lead to the development of food yeasts which contain less purines. Numerous methods have been developed for incorporating yeast in breads, soups and other foods. The greatest need for food yeast would appear to be in India, in China and in the tropics where population pressure on the land or economic conditions or both are great enough to make impossible provision of enough meat and milk to supply the population with protein of high biologic quality. The cost of yeast is small, and addition of it in amounts not more than 3 per cent might help enormously when diets are strictly vegetarian.

Cultures of other micro-organisms may serve as protein food for man. Fusarium lini Bolley with a supplement of thiamine provided adequate amounts of the B complex vitamins for the normal growth, reproduction and lactation of mice. Fed to mice as the only source of protein at a 15 per cent protein level, growth was as satisfactory as with 18 per cent of casein. The possibilities as foods of this Fusarium and related molds appeared to Vinson and his colleagues to be important, for they can be easily grown in the course of the alcoholic fermentation of the 6 and 5 carbon atom sugars present in wood hydrolysates, sulfite waste liquors and silage.

FOODS FOR RELIEF

Foods best adapted for stockpiling or for shipping to areas in need of relief must be relatively imperishable and largely free from water. In the emergency of any war or major social turmoil, transportation at once becomes a problem of immense importance. Freight cars and ships in wartime are in great demand for moving troops and military stores, and the facilities that can be obtained for moving food are rarely ever adequate to meet requirements fully. Moreover, transportation is peculiarly sensitive to enemy attack. In

Germany, near the war's end and later in the occupation period, collapse of transportation contributed as much or more to famine as did shortage of the total food supply. White flour, white rice, degerminated corn, sugar and fats and oils best meet requirements for stockpiling and shipping. They, however, for the most part are poor providers of minerals, vitamins and the better proteins. Among foods best suited to supply these factors are cheese, dried beans, dried peas and dehydrated (or for certain purposes canned) milk, eggs, meat and fish.

Canned food has played a role in every recent war, but never a greater one than in the war just passed. Its contribution to maintaining the nutrition both of the military and civilian populations of this country and of our allies was tremendous. Canned milk, canned meat, canned fish and great varieties of canned vegetables and fruits were shipped to all parts of the world in quantities as large as means of transportation would permit. From the standpoint of imperishability and good nutritional quality, foods preserved by modern canning methods rank among the best. They also lend themselves to stockpiling. Their only disadvantage is that their weight and bulkiness complicate their transportation.

Dehydration as a means of saving shipping space represented a major contribution in solving the problem of providing Britain with food enough to keep its people fed in World War II. In the years before the war about 3,000,000 tons of water were imported into Britain. This was contained in the food that came from overseas. Much of that wasted effort was overcome by shipping foods from which the water in large part had been removed. Eggs were dried. Before the war British imports included 2,000,000,000 eggs, of which 75 per cent (or 100,000 tons) was water. Fresh meat for transport overseas called for refrigerated ships, whereas dried meats could go in any kind of boat. Dried soups were shipped in quantity. Cheese and butterfat were in great demand as shipping items, since they were relatively free of water. Powdered egg was produced and shipped in enormous quantities. It proved unsatisfactory until methods were developed which insured good solubility. With the better products which eventually were provided, omelets, cakes and custards could be made which equalled those prepared with fresh eggs. However, the most important items in this category were evaporated milk and dried skim milk.

Milk.—Wherever liquid milk can be obtained it represents a most acceptable and satisfactory means for obtaining protein of high biologic quality. Goat's milk possesses about the same nutritive properties as cow's milk, but goats can thrive in rocky country where cows do poorly. In such places raising goats for local consumption of their milk and meat has been encouraged. Fluid milk, however, because of bulk and perishability, is expensive to transport to distant regions. The handicap is largely overcome by processing before shipment. Evaporated milk, dried milk and many forms of cheese are relatively imperishable, occupy relatively little shipping space and compared to fluid milk can be delivered to a distant market at a relatively low cost.

Dry milk, either dry whole milk or dry skim milk, has come to play a part of great importance in feeding undernourished people. Its value in the treatment of the famished inmates of Nazi concentration camps was discussed by Pollack. It is excellently suited for constructing diets high in protein. For this purpose it can be mixed with other foods in large proportions or made into a paste by adding 1 part of dry milk powder to 2 parts of water. Whole liquid milk or buttermilk or orange juice may be used as the diluent. Flavoring can be added if desired, and added egg or powdered egg gives the mixture a custard character with additional nutritional advantages. With these products now becoming generally available there is little need for any of the various protein concentrates of fancy composition appearing in the drug trade or for the protein hydrolysates which recently have been promoted for oral use. There is little evidence that any of these products are absorbed more readily than milk even when digestion is impaired. Their cost is out of sight and the atrocious palatability of protein hydrolysates makes them unacceptable even when administered by stomach tube.

Among milk products of great usefulness as a source of protein in the war was cheese, which rivals any food available as a source of protein, is relatively imperishable and lends itself to shipping. Very large amounts of American cheddar cheese have been exported and production in this country has increased accordingly. American or cheddar cheese has represented about 80 per cent of a total cheese production, which now is said to utilize annually about 10,000,000,000 pounds of milk. An economic as well as dietary objection to converting milk to cheese is the loss of whey, which contains the lactalbumin of the milk, some of its mineral and much of its vitamin content. Uses for whey have been difficult to develop, and to waste this highly nutritious material is well-nigh criminal. Whey can be dried to powder and used advantageously in bread making much as has been done with dry skim milk. It also can be used in candy manufacture, but other outlets ought to be explored.

FATS AND OILS

A major problem in all the war-torn countries, and not without real significance in North America, was the shortage of fats occasioned by the war. This developed from two causes: (1) the interruption of imports of coconut, palm and other oils from the Pacific islands, and (2) the demand for oil and fat for war use.

While the evidence for a minimal fat requirement is inconclusive, the opinion prevails that 20 to 25 per cent of the total calories should come from fat. Half of this total usually should be obtained in a visible form as butter, lard and oil. The total would amount to from 54 to 68 pounds (24.5 to 30.8 Kg.) per year, whereas the per capita prewar consumption in the United States was 93 pounds (42.2 Kg.). The principal sources of invisible fat are dairy products other than butter, meat, nuts and eggs. The supply of them as well as the supply of fats and oils has been short in Europe since the war began. Much could have been done to alleviate postwar shortage of fat in Europe had the United States adopted a more enlightened program for its use of fats and oils during the war years. Because of their relative imperishability fats and oils can be stockpiled over years. However, such a program involved restriction of the use of fat for soap and for military purposes, and resistance was strong enough to prevent any such restrictions.

FOOD MANAGEMENT

The successful prosecution of World War II depended to a large extent on the herculean efforts of farmers and other food producers in the United States and Canada. Blessed by successive years of better than average growing weather, food production was increased almost a third and much of the increase became available for

export. A further vital contribution involved measures that were introduced for managing distribution, "set-asides" of food commodities, price control and differential rationing. This is not the place for discussion of food management over the world. In due time the story will be told by the Food Research Institute of Stanford University, which has received a large grant of money from the Rockefeller Foundation for a five year study of the subject. Some account of procedure in the United States has been given by Hendrickson and by Clayton and Black. An account of procedure in Canada has been published under the authority of the Minister of National Health and Welfare. The experience of Switzerland has been reported in a recent monograph by Fleisch, and separately under the auspices of the Food Research Institute by Rosen.

By careful management of their food supplies the Swiss and British came through the war without deterioration, and indeed in many respects with actual improvement of the public health. Sir William Jameson, British Minister of Health, could state in 1946 that infant mortality rates and puerperal death rates had fallen steadily. The problem of nutrition in Great Britain received interesting consideration in a recent book by Cruickshank. In Switzerland, despite lowering of food supplies and shortages of protein and fat, the heights and weights of children were maintained. The incidence of most reportable infectious diseases was diminished, as was that of diseases of the gastrointestinal tract, including appendicitis.

SUMMARY AND CONCLUSIONS

For populations in the path and in the wake of war, finding food becomes a matter of supreme importance. By utilizing edibles which in normal times are disregarded, much can be done to alleviate or postpone the worst effects of famine. Substantial contributions to the family larder can be made by gardening. By these means sufficient vitamins and minerals are usually obtainable. The pressing problems, then, relate to calories and biologically superior protein. Cereal grains, wheat, corn, barley, oats and rye are efficient providers of calories and possess the advantage of being readily transportable. However, the proteins of cereals and vegetables fail to provide all the amino acids necessary; moreover, a need for fat, which apparently is very real, cannot be met with cereals and vegetables alone. Therefore, planning to meet the food needs of countries overrun by war, likewise to meet the needs of areas like India where population pressure excludes the use of land for producing meat and milk, involves attention to supplies of protein and fat. Certain resources, especially fish, can be made to contribute more abundantly. Food yeast offers possibilities. Yeast and beans, soy beans in particular, afford proteins which when taken with wheat flour or white rice are reasonably complete. Fat production can be augmented by increased planting of "oil seeds" such as soy beans, peanuts, rape and okra, and fat can be diverted from other uses in order to increase the amount available for food. Foods for distant shipping in conditions of emergency, likewise foods which lend themselves to stockpiling, must be low in water content and relatively imperishable. White flour, white rice, sugar and fats and oils best meet such requirements. They, however, for the most part are poor in minerals, vitamins and superior proteins. Among the foods best suited to supply these factors in emergencies are dehydrated milk, cheese, dried eggs and fish.

Clinical Notes, Suggestions and New Instruments

GRANULOMA INGUINALE OF THE VAGINA AND CERVIX UTERI WITH BONE METASTASES

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Since McLeod's description in 1882 of granuloma inguinale as a "serpiginous or lupoid ulceration of the genitalia," this disease has been more clearly differentiated from other granulomatous lesions of the genitalia and the vagaries of its clinical manifestations have received increasing attention. Earlier concepts of the progress of this infection solely by serpiginous spread or by autoinoculation have been broadened in recent years as a result of accumulated evidence of lymphatic spread and involvement.[1] Examples of the latter are the inguinal "pseudobubo" [1a] following the primary genital lesion, the demonstration of the Donovan bodies in regional lymph nodes [1a, b] and the elephantiasis of the genitalia [2] which may occur in this disease. To lymphatic spread has also been attributed the extensive involvement of the pelvic organs following granuloma inguinale of the cervix and vagina.[3] Of significance are the pronounced systemic manifestations which are frequently associated with lesions in this region, particularly when complicated by pregnancy.[4] These systemic manifestations indicate that granuloma inguinale, far from being strictly a local disease of the genitalia, has potentialities for widespread dissemination throughout the body, either of the specific etiologic agent or the products of secondary invaders. The former possibility has already been demonstrated by a few reported cases of metastatic lesions of bones and joints in distant parts of the body following lesions of the genitalia.[5] Thus has evolved from the early beliefs of the limited implications of this disease a clearer understanding of the possibilities for widespread dissemination which this disease possesses.

The case of granuloma inguinale to be reported is of interest in view of the simulation of a carcinoma of the cervix, the profound systemic manifestations, the metastatic bone lesions and subcutaneous abscesses at a distance from the site of the primary lesion and the demonstration of organisms having the morphology of Donovan bodies in blood culture.

REPORT OF A CASE

A Negro woman, aged 19, was admitted to the maternity service of John Gaston Hospital Feb. 21, 1946, with a tentative diagnosis of threatened abortion and with evidence of pneumonia of the upper lobe of the right lung, which was later confirmed

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by roentgen observations. Subsequently she admitted having passed some "flesh" from the vagina the day before entering the hospital, so that it is likely that a complete or incomplete abortion had occurred before admission. She responded well to sulfadiazine therapy and was discharged in afebrile condition from the hospital on the ninth day.

She returned to her work in a restaurant and worked for one week. She was obliged to discontinue work at this time because her left hip had become painful and swollen so that she was unable to walk. She also had some discomfort in the right lower quadrant of the abdomen and in the back at this time.

During the next seven months she was confined to her home at a result of these complaints, spending most of her time in bed. She had no menstrual periods, and lost 60 pounds (27.2 Kg.) in weight (from 150 pounds [68 Kg.]) over this period. She was seen in the outpatient department in July, and at that time a woody induration of the left anterior wall of the vaginal vault was noted, with no involvement of the cervix. A diagnosis of streptococcic infection of the vagina and adnexa was made.

Four weeks before her second admission to the hospital she began passing bloody urine containing clots, accompanied by dysuria. The pain in the lower part of the abdomen became more severe at this time, and she also noted a bloody vaginal discharge.

She was admitted to the hospital for the second time on October 6. On admission her temperature was 102.4 F., pulse rate 100 and respiration rate 26. Blood pressure was 100 systolic and 60 diastolic. She was rather emaciated and appeared to be weak. Among the significant findings at this time were tenderness in the lower abdominal quadrants and the presence of a tender, nodular, friable infiltration of the cervix and lateral and posterior walls of the vagina. Bimanual examination was unsuccessful because of the extreme tenderness and the "frozen" condition of the pelvic organs due to parametrial and adnexal thickening. Rectal examination also produced excruciating pain.

Laboratory examination on admission revealed a red blood cell count of 3,700,000 per cubic millimeter, a hemoglobin level of 10.0 Gm. per hundred cubic centimeters and a white blood cell count of 20,250 per cubic millimeter with 84 per cent polymorphonuclear leukocytes. The corrected sedimentation rate was 31.5 mm. in sixty minutes. The urine showed albumin

Fig. 1.—Bone changes underlying subcutaneous abscesses. The distal end of the second metacarpal bone shows rarefaction with extensive periostial proliferation. The tibia shows an area of rarefaction on the medial surface of the condyle.

(3 plus) with innumerable white and red blood cells. The Kahn test report was 3 plus. Frei, Ducrey and tuberculin cutaneous tests were negative in result. A roentgenogram of the chest revealed no abnormality. Two routine blood cultures and routine agglutination tests were also negative in result.

Soon after her admission to the hospital, a perirectal abscess developed, which was incised and drained, with the evacuation of sanguinous pus. Soon after this she complained of pain in the right knee and in the knuckle of the left hand. No swelling was noted, and the pain soon subsided. Two weeks later the pain recurred in the same regions, this time being associated with definite swelling and local tenderness. Again these signs and symptoms subsided, only to recur two weeks later, progressing this time to form large fluctuating abscesses beneath the skin, which appeared normal. These abscesses were incised.

Fig. 2.—Pathognomonic cell of granuloma inguinale, obtained from abscess of the hand. The macrophage cell contains a cyst or "nest" of closely packed Donovan bodies. In the cytoplasm of the macrophage cell individual Donovan bodies show the typical encapsulated, safety pin forms.

The pus was cultured by routine procedures, but nothing could be grown. Tender swellings of the dorsum of the right hand and of the left elbow also appeared at this time, but did not progress to suppuration. Roentgenologic examination of these areas revealed areas of bone destruction under each swelling noted before. The right tibia showed an area of destruction 2 cm. in diameter on the medial surface of the condyle. This area of necrosis was surrounded by a rim of sclerosis. In the distal end of the shaft of the second metacarpal bone of the left hand was a cystlike area of rarefaction with extensive periosteal proliferation (fig. 1). The navicular bone of the right hand showed an area of destruction involving one half of this bone.

A cystoscopic examination was performed because of the urinary complaints present at the time of admission. This revealed a granulomatous lesion of the bladder, involving the floor and left wall. There was some obstruction of the left ureteral orifice, with hydroureter and hydronephrosis on that side. The impression was that of an extensive malignant growth, originating from the cervix uteri and spreading to involve the bladder.

Biopsies of the cervix uteri revealed numerous large macrophages, suggesting the possibility of granuloma inguinale. Intensive search for the Donovan bodies revealed them in the hematoxylin and eosin preparations, although they appeared rather pale and were seen only with difficulty in these preparations. Preparations stained with Giemsa or with Dieterle's silver stain demonstrated the Donovan bodies more clearly. What we considered to be the most satisfactory preparation of all in demonstrating the Donovan bodies was obtained by simply smearing a particle of granulation tissue on a slide and staining by Wright's technic, as for blood smears. Contact smears of the granulation tissue at the sites of the incisions

of the left hand and right knee stained by the latter procedure also revealed these organisms in profusion in macrophage cells (fig. 2).

A blood culture employing tryptose-peptone-egg yolk agar showed organisms morphologically resembling Donovan bodies. This, together with observations made with an antigen obtained from pus from one of the abscesses, is being reported separately.[6]

Response to intravenous injections of antimony potassium tartrate was dramatic. The initial dose was 3 cc. of a 1 per cent solution. Subsequently the dose was given every other day, increased by 1 cc. each time until the tolerance level of 8 cc. was reached. Within a week the temperature receded to normal, appetite improved and weight gain was noted. During the next three weeks a gain of 20 pounds (9.1 Kg.) in weight was made. The granulation tissue in the vagina became firm in consistency and shrank in size so that only a small area of the cervix was involved. Granulation tissue at the site of the incisions in the hand and knee healed more slowly, and Donovan bodies could be demonstrated in this granulation tissue twenty-four days after treatment was initiated. Forty days after treatment was started the typical encapsulated Donovan bodies were no longer observed, but in a few macrophages there could still be seen clumps of nonencapsulated organisms, similar in appearance to Donovan bodies. The patient was discharged from the hospital with advice to continue her treatment in the outpatient department.

COMMENT

This case is of interest from the standpoint of providing additional evidence of the capacity for widespread systemic invasion inherent in granuloma inguinale of the cervix uteri. While bone metastases as described in this case have rarely been reported in the literature, it is conceivable that they have occurred more frequently than has been recognized and that they have been mistaken for cancers of the cervix with bone metastases. The possibility of confusing, on clinical appearance, granuloma inguinale of the cervix with a malignant growth of that site can readily be understood, as it is doubtful whether these can be distinguished on clinical grounds alone. What cannot be condoned is the treatment of such cases as cases of malignant growths without substantiating histologic findings, on the grounds that the biopsy may not have been correctly taken and that the clinical evidence of cancer was so overwhelming.

Attention should be called to the fact that in biopsy material the possibility of granuloma inguinale should be suspected when large numbers of large macrophages are present. The diagnosis can then be verified by the careful study of tissues for the presence of the Donovan bodies. Since these bodies are most readily seen in contact smears stained by the Wright technic it is always advisable to supplement the biopsy study with this procedure when feasible. This is especially indicated when lesions of the cervix suspected of being malignant fail to reveal evidence of being so on biopsy study.

The dissemination of the infection, with systemic manifestations, which occurred in our patient after an abortion emphasizes the hazard which pregnancy holds for patients with granuloma inguinale of the cervix. This hazard has been emphasized by others,[1d] who have reported widespread pelvic involvement and death following such a complication. The importance of having a high index of suspicion for granuloma inguinale in the presence of lesions of the cervix in pregnant women is obvious.

The occurrence of bone lesions in this patient at sites commonly involved in hematogenous spread of infection justifies the assumption of hematogenous dissemination of the etiologic agent. In no instance was there any evidence of involvement of the skin at the site of the fluctuating abscesses prior to their incision. This rules out the possibility that autoinoculation played a role in producing these lesions at a distance from the original site of involvement. The failure to demonstrate common organisms by routine blood culture and the demonstration in blood culture of organisms having the morphologic appearance of Donovan bodies would appear to confirm this opinion. We were unable to find any other instance reported in the literature in which Donovan bodies have been observed in blood culture. Failure to observe continued growth in the medium employed indicates that this medium is not a suitable one for the continued propagation of this organism.

6. Dulaney, A. D., and Packer, H.: Complement Fixation Studies with Pus Antigen in Granuloma Inguinale, Proc. Soc. Exper. Biol. & Med. **65**: 254 (June) 1947.

SUMMARY

A case of granuloma inguinale is described in which the initial involvement of the vagina, cervix and bladder was subsequently followed by bone metastases with overlying abscesses in distant parts of the body.

The progress of the infection, with profound systemic manifestations, following an abortion emphasizes the hazard of pregnancy for women with untreated granuloma inguinale of the cervix.

The sites of bone involvement and the deep tissue suppuration arising therefrom suggest hematogenous spread of the etiologic agent in this case. The demonstration, the first which we have been able to find in the literature, of organisms having the morphologic appearance of Donovan bodies in blood culture on special medium substantiates this impression.

The unreliability of routine hematoxylin and eosin preparations of biopsy material in demonstrating clearly the Donovan bodies is pointed out.

Attention is called to the fact that granuloma inguinale of the cervix uteri may simulate a carcinoma in appearance. It is recommended that in the examination of lesions from the vagina and cervix for suspected malignancy smears be obtained from the surface of the lesion, or from particles of granulation tissue, and stained with Wright's stain. This rapid simple procedure might well be placed on a routine basis in population groups in which granuloma inguinale is known to occur.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

CHORIONIC GONADOTROPIN (See New and Nonofficial Remedies, 1947, p. 374).

The following additional dosage form has been accepted:

GEORGE A. BREON & CO., KANSAS CITY, MO.

Chorionic Gonadotropin, 5,000 International Units and 10,000 International Units: 10 cc. vials. A powdered preparation which, when diluted with the accompanying 10 cc. vial of sterile distilled water containing 0.2 per cent metacresol, provides a solution having a potency of 100 or 500 international units, respectively, per cubic centimeter.

TYPHOID VACCINE (See New and Nonofficial Remedies, 1947, p. 462).

The following dosage form has been accepted:

PITMAN-MOORE COMPANY, INDIANAPOLIS

Typhoid Vaccine: 5 cc. and 20 cc. vials. Each 1 cc. contains 1,000 million killed typhoid bacilli (Panama carrier strain 58). Preserved with sodium ethyl mercuri thiosalicylate 1 : 10,000.

STERILE SULFADIAZINE SODIUM (See New and Nonofficial Remedies, 1947, p. 141).

The following dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Sulfadiazine Sodium (Sterile Powder): 5 Gm. ampuls.

EPHEDRINE SULFATE (See New and Nonofficial Remedies, 1947, p. 214).

The following dosage form has been accepted:

THE S. E. MASSENGILL COMPANY, BRISTOL, TENN.

Solution Ephedrine Sulfate, 3 per Cent: 473 cc., 120 cc. and 30 cc. bottles. Preserved with 0.5 per cent chlorobutanol.

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SATURDAY, JANUARY 31, 1948

WHEAT AND WORLD HUNGER

Why do we send wheat as a most important article of diet to the hungry people we are trying to help? The high food value of wheat per unit of weight, its excellent keeping qualities, its ease of handling and storing make it ideal for shipping; further, wheat satisfies hunger as do few other foods. Why is wheat the dominant food grain—the grain of choice for bread? The answer rests chiefly in two factors: (1) properties inherent in wheat itself and (2) the widespread, general insistence on wheat and its milled products.

Aside from certain areas of Monsoon Asia where agricultural factors and habits observed for centuries have combined to establish rice as the dominant food grain,[1] five cereal grains—wheat, corn, oats, barley and rye—constitute the principal grain crops. Except for certain differences in quantitative aspects, all cereal grains exhibit similarities in composition and nutritive value. Some of these quantitative differences, however, are not without significance; for instance, the association of pellagra with the consumption of high proportions of whole ground cornmeal.

Wheat, among the five principal grains grown in Western countries, embodies most of the superior qualities of each of these common grains. It is not bulky, thereby minimizing the costs of handling; as whole grain or white flour it has excellent keeping qualities; by virtue of the rather unique quality of its protein (gluten), wheat flour is preeminently suited for making yeast-leavened breads.

The present shortage of wheat concerns physicians throughout the world because it stands as a stark barrier to the relief of world hunger and as an obstacle to world economic recovery. Never before has relief from hunger of so many millions of persons been so contingent on available supplies of a single food item.

Why is there a world wheat shortage? In spite of the devastations of World War II, the Western countries of Europe demonstrated remarkable powers of recovery in wheat production in 1946. The reverse in this trend in 1947 was caused principally by unfavorable weather conditions for growing wheat in several Western and Southern European countries. Wheat reserves in recent years have been absent in practically every country that normally produces a surplus of the grain.

The principal non-European wheat-exporting countries include Australia, Argentina, Canada and the United States. Australia's wheat exports, although important, are relatively small; Argentina's wheat exports are under government monopoly, with insistence on payment in American money at the highest price of wheat on the world market; Canada's exports are destined largely for Great Britain. This leaves the United States to fill the gap as far as possible. In those countries where the demand for wheat imports has not been satisfied, the strain on other available food supplies has been stretched to the limit; demand for food has overwhelmed supply; food prices have skyrocketed except where controlled; black markets in foods tend to flourish so that whole national economies are disrupted by present food shortages.

Why not spread the strain to other grains or to other foods than wheat? Few countries produce surpluses of any food. In Western Europe many countries are deficient in several staple foods. The use of fruits and vegetables is largely precluded in the relief of mass hunger by their bulk, high water content, easy spoilage, inflated prices and high cost of transport by rail and water. Some dehydrated foods are being sent to Europe, but the quantities available are not significant. Small amounts of meat, dehydrated eggs and milk are also being sent to European countries. However, all profitable and large scale production of top quality meat, dairy or poultry products requires grain. Shortage of feed grains, such as now exists in this country, should tend to be balanced by appropriate reductions in live stock. There is no escape from the fact that cereal grains (food or feed grains) used directly and indirectly as food are the bulwark of sustenance for most of the world's human population. The excessive production of animal-converted foods—especially top quality meats which require extra grain for fattening—is a waste of food calories during a world food crisis. Less expensive cuts of meat contain relatively more protein per unit of weight, are equally nutritious and require much less grain in their production.

In the forthcoming edition of the "Handbook of Nutrition" of the Council on Foods and Nutrition other aspects of the problem of the relation of wheat to human nutrition will be discussed. Some of the chapters will appear first as special articles in The Journal. Maynard of Cornell will describe the contribution of foods of plant origin to the human diet, Ancel Keys will discuss starvation and Wilder and T. E. Keys (this issue, p. 322) the role of foods for emergencies. Now more than ever before a knowledge of nutrition is significant not only for individual health but for the future of the world.

1. Millet and buckwheat (not properly a cereal grain) continue in general use in a few regions.

GENETIC CONTROL OF LYMPHOMATOSIS IN THE FOWL

Neoplastic diseases are not exclusively a problem in man; lymphomatosis in fowl causes an annual loss in this country of $50,000,000.[1] Forty per cent of the high mortality in growing fowl during the first year of life results from lymphomatosis. The disease is characterized by a proliferation of undifferentiated lymphocytes in the viscera, nerves and iris; it is transmitted to fowl under 5 months of age by contact with older stock. Since lymphomatosis is transmissible by cell-free filtrates it is presumably a virus disease, neoplastic in character.

Hutt and Cole[2] controlled the disease by genetic methods. In twelve years they developed from a previously unselected population two strains of fowl resistant to the disease. Other desirable features such as satisfactory body size, egg size, and egg production were not lost in the process. Simultaneously, by the same genetic methods, a strain highly susceptible to lymphomatosis was produced, despite the fact that selection was less efficient. In the resistant strains mortality from the neoplasms was reduced to about one third its original figure; in the susceptible strain it was doubled. The latter strain now has a tumor mortality of over four times that of the resistant strains under identical conditions of exposure.

Records of breeding were kept, including the ancestry of each chick; uniform environment was maintained and equal natural exposure to lymphomatosis was insured. The sires and dams whose production of the most resistant families had been proved were selected for breeding. Not only was mortality from lymphomatosis reduced but that from other causes as well. Decreased mortality from lymphomatosis was accompanied by an increase in average age at which the disease appeared.

After the desired lymphomatosis-resistant stock was developed, the next problem concerned utilization of the fowl to best advantage. The investigators concluded that the best method would be to send the desirable genes of the resistant strains in thousands of cockerels to head flocks that supply the hatcheries that now produce about 90 per cent of the country's chicks.

While this method of attack on a problem in neoplastic disease is interesting, similar genetic methods are not, in the present state of society or in the near future, applicable to problems in human disease. Furthermore, there is no known human neoplastic disease comparable to this form of lymphomatosis in fowl. The human malignant lymphomas have to date revealed no transmission by contact, transmission by cell-free filtrates or high incidence in certain families. In these respects the lymphomatosis of fowl resembles an infectious disease and the methods used in its control were those applicable to some infectious diseases of animals but not to those of man.

1. Winton, B.: Fourth Annual Report of the Regional Poultry Research Laboratory, East Lansing, Mich., United States Department of Agriculture, Washington, D. C., Government Printing Office, 1943, p. 3.
2. Hutt, F. B., and Cole, R. K.: Genetic Control of Lymphomatosis in Fowl, Science **106**: 379-384 (Oct. 24) 1947.

THE PAPANICOLAOU TEST FOR UTERINE CANCER

Early diagnosis of uterine cancer has depended chiefly on the subjective symptoms of the disease. Often the disease is far advanced by the time the patient becomes sufficiently aware of discomfort to seek help. Study of the normal and abnormal variations in the vaginal smear in guinea pigs and in women convinced Papanicolaou that carcinoma of the fundus of the uterus and carcinoma of the cervix are to some extent exfoliative lesions. Cells at the free surface of the growth tend to become dislodged and subsequently to find their way into the vagina. Papanicolaou developed a method for collecting the cellular débris, which is smeared on glass slides and specifically stained so that the various components may be studied. In their first report on the method, Papanicolaou and Traut[1] emphasized that "whereas the method makes the material for examination easily and frequently obtainable at low cost, the interpretation of the smear requires the services of a careful and discriminating cytologist who has had experience in this field. Few persons can be depended on for this work at the present time."

Cervical cancer is revealed in vaginal smears by the appearance of characteristic cells derived from the superficial layers of the tumor, which undergoes continual desquamation. These cells show great variety in form and size, much greater than that seen in sections of the tumor. The most characteristic feature of the abnormal cells is the atypical form and structure of their nuclei and vacuolization of the cytoplasm. A commonly found, characteristic cell type is an extremely elongated one resembling a smooth muscle fiber. Erythrocytes are generally found in large numbers. Papanicolaou and Traut, utilizing the vaginal smear technic, failed to detect malignant cells in 4 of a total of 127 patients with demonstrable cancer of the cervix. They found cancer cells in the vaginal smears of 46 of 53 patients with cancer of the fundus.

Meigs and his associates[2] reported 4 positive smears in a total of 153 negative cases, an error of 2.6 per cent. Of 46 patients with proved cancer of the cervix, positive vaginal smear diagnosis was made in 45, an error of 2.2 per cent. These authors expressed their belief that a cancer cell can be more readily identified in the vaginal smear than in body fluid sediments or sputum. This increased accuracy in diagnosis is proba-

1. Papanicolaou, G. N., and Traut, H. F.: The Diagnostic Value of Vaginal Smears in Carcinoma of the Uterus, Am. J. Obst. & Gynec. **42**: 193 (Aug.) 1941.
2. Meigs, J. V., and others: The Value of the Vaginal Smear in the Diagnosis of Uterine Cancer, Surg., Gynec. & Obst. **77**: 449 (Nov.) 1943.

bly due to the fact that cells of the vaginal fluid are in greater concentration and have suffered less degeneration. These authors did not feel justified in advising operation for uterine cancer solely on the evidence of a positive vaginal smear. They insisted that the positive smears should be confirmed by biopsy or curettage. They also emphasized the need for a systematic study of the entire smear and an experienced knowledge of cytology. The method of vaginal smear examination, in their opinion, is an important addition to the early recognition of uterine cancer.

Block [3] has warned that a positive diagnosis from a vaginal smear does not indicate immediate radical intervention or irradiation, but rather that confirmatory biopsies of the cervix or endometrium should be performed.

Scheffey and Rakoff [4] deplore in a recent communication the exaggerated statement that appeared in the Sept. 19, 1947 issue of the *New York Times* regarding the cytologic test for uterine cancer. "The message of hope" reported in this article was condensed from an article by Clive Howard in the October 1947 issue of the *Woman's Home Companion*. According to this article "the new method is inexpensive, painless and at least 97 per cent accurate. If put into general use it may almost wipe out this form of cancer." The danger was the creation of a tendency to depend on a laboratory examination rather than on a complete study of the condition. The report does not stress that a positive smear must be confirmed by cervical biopsy or resection and/or by curettage of the uterine cavity. The article was completely laudatory except for mention of the 3 per cent error of the investigators. Scheffey and Rakoff found in a study of 500 consecutive cases, taking only a single smear and without clinical knowledge of the cases on the part of the cytologist, that of 63 proved cancer patients correct positive smears were obtained in 44, or 70 per cent. In other words, 30 per cent of the cancer cases were missed. Excellent correlation, however, was obtained in 437 patients who did not have carcinoma, correct smears being obtained in 430, or 98.4 per cent, while false positives occurred in only 7, or 1.6 per cent. Apparently, therefore, the good results for the entire group, namely 98.4 per cent correct results, were influenced largely by the high proportion of negative patients. In studies by other workers false positives were comparatively rare but positive cases were missed in an appreciable proportion of the cases. The limitations of the vaginal smear method, especially when only one smear is taken, are obvious.

Recently a manufacturer of laboratory equipment has promoted the sale of the materials for the Papanicolaou test together with a hundred slides of various types of cells found in cervical smears. The firm cannot, however, sell the most important ingredient—a competent pathologist to study the specimen promptly after it is secured from the patient. The offer implies that special training is not necessary to secure and to examine the specimen. The indiscriminate use of this test will result in more harm than good.

3. Block, F. B.: Cancer of the Cervix, Am. J. M. Sc. **208**: 794, (Dec.) 1944.

4. Scheffey, L. C., and Rakoff, A. E.: The Cytology Test for Uterine Cancer, Philadelphia Med. **43**: 435 (Nov. 15) 1947.

Current Comment

CHECKING THE SPREAD OF YAWS ON PACIFIC ISLANDS

On the numerous small islands in the Pacific Ocean within a few hundred miles of the atoll of Truk, thousands of the inhabitants are afflicted with yaws, an infectious disease caused by the Treponema pertenue (Spirochaeta pertenuis) and resembling syphilis in some of its manifestations. The people on these islands now receive medical care by U. S. Navy personnel [1] from the Truk atoll; a medical team visits them every six weeks. The lack of personnel and ships and the distances led the navy physicians to try a single intramuscular injection of 200,000 units of sodium penicillin in 4 cc. of sterile water as a stopgap measure to check the spread of yaws. As it became available toward the end of the program, a single injection of 300,000 units of calcium penicillin in 1 cc. of beeswax and peanut oil was substituted. The persons treated numbered about 5,000. The careful records kept for the period from October 1946 to June 30, 1947 show that the rate of infection with yaws has been much reduced. The thirteen small islands south and east of Truk showed a reduction, over a period of six months, from 57 new cases per thousand per month to 16 new cases per thousand per month. The total number of clinically active cases was also reduced. At the same time the character of the lesions commonly present in those afflicted has changed. When this program began in 1946, the ratio between the open cases, with ulcers, and the closed cases was about one to two. In June 1947 the major portion of the total number of cases still active was of the "crab yaws" variety, the less infectious type. Since last July the islands south and east of Truk have been staffed with native health aides trained to give oxophenarsine hydrochloride ("mapharsen") and bismuth compounds and thus carry on curative treatment. Curative therapy with penicillin, which would be more satisfactory, cannot be instituted because of the lack of refrigeration facilities on the islands. However, the single massive dose therapy with penicillin will be continued on the islands north and west of Truk until they too can be staffed with natives trained in the application of curative therapy. Thus it appears that a single intramuscular injection of a massive dose of penicillin is effective in checking the spread of yaws and in controlling the active cases until curative therapy can be instituted. The U. S. Navy is to be congratulated on its effort to prevent the spread of a deforming and disabling infectious disease, which is particularly prevalent among members of the dark races of the tropics.

1. Arje, Sidney L. (MC), U. S. N.: Yaws Treated with Single Massive Doses of Penicillin, United States Naval Medical Bulletin **47**: 966-969, (Nov.-Dec.) 1947.

ORGANIZATION SECTION

Official Notes

HOTEL RESERVATIONS FOR THE ANNUAL SESSION IN CHICAGO, JUNE 21-25, 1948

A list of hotels in Chicago and information concerning the best way to secure hotel reservations for the Annual Session, to be held in Chicago June 21-25, 1948, may be found on advertising pages 56 and 57 of this issue of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. The meetings of most of the sections will be held on Navy Pier.

It is urged that physicians expecting to attend the annual session in Chicago fill in the application form to be found on the advertising pages indicated, sending it to Dr. Fred H. Muller, Chairman of the Subcommittee on Hotels of the Local Committee on Arrangements, 195 West Madison Street, Chicago 2.

Medical Economics

THE SELLING PRICE OF A MEDICAL PRACTICE

FRANK G. DICKINSON, Ph.D.
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Chicago

Some time during his professional career, a physician may face the problem of buying or selling a practice. After the physician completes his internship or residency, he may consider purchasing the practice of an older physician. After establishing himself in private practice, he may for various reasons contemplate a change of location, involving both the sale of his own practice and the purchase of another elsewhere. Following the retirement or death of a physician the sale or disposal of his practice may be considered.

The sale or purchase of a medical practice raises many questions; a considerable number of requests for information and advice are received at the headquarters of the American Medical Association. Perhaps the most frequent question concerns the means of establishing a proper selling price for a practice. But little has been published on this subject recently. Thoroughgoing studies have not been made of either the economic or legal aspects; nor have there been any compilations of actual experiences. The Bureau of Medical Economic Research recently conducted an informal survey among secretaries of state medical societies and accumulated available facts from other sources.

SALE OF PRACTICES IN ENGLAND

In England the custom of selling medical practices for prices significantly above the value of equipment, supplies and other tangibles has long prevailed. A special circumstance exists in England and possibly in other countries where panel practices have been established as a result of the operations of sickness insurance systems. The following brief description of this custom was received in a communication from an authoritative source in London:

> The sale of the goodwill of general medical practices in England is based on a figure related to the past earnings of the practice and to the estimated receipts from continuing patients. In all cases the gross earnings for one year (or the average gross earnings for two or three consecutive years) is taken as the basic figure from which to work. This figure is multiplied by the number of years' purchase agreed between the vendor and the purchaser. In the years preceding the outbreak of war in 1939 this factor varied between one year and two and a half years, the lowest figure being that obtainable in the least satisfactory circumstances such as the death of a man in singlehanded practice where there was no opportunity for the newcomer to be given any introduction to the patients. The price increased directly with the degree of probability of transfer of the patients of the vendor to his successor. Experience has shown that state patients on the doctors' Panel Lists only infrequently exercised their right to transfer to another doctor rather than accept the services of the purchaser of their former doctor's practice. In consequence practices with a high proportion of state patients tended to change hands for slightly more than ones in which there was less certainty of the continued adherence of private patients.
>
> On the average, a well established practice, where there was good opportunity to introduce a new partner, sold at about two years' purchase.

Another correspondent reported that this custom applies basically to general practices, although the goodwill of ophthalmic and radiologic specialists also may be sold. Unpaid bills may or may not be included in these transactions. In addition, it is usual to make a separate valuation of the "capital" of the practice, which would include drugs, supplies and equipment. This writer emphasized that it is not patients but goodwill that is sold.

AVAILABLE INFORMATION AND SUGGESTIONS

Current information concerning physicians' practices which are for sale may be obtained from several sources. A few state societies reported that they occasionally provide clearing-house facilities between parties; possibly most other societies would be willing to furnish available information. The medical journals are probably the most important source for such opportunities—including the classified advertising sections of local, state and national publications. Other avenues of approach for either the buyer or seller are medical placement agencies and inquiries among professional acquaintances. In addition, a physician wishing to purchase a practice may offer an advertisement.

Many of the secretaries of medical societies commented on the factors to be evaluated in ascertaining the selling price of a practice. Most of them considered that the tangible goods could be appraised readily but suggested that pricing of intangibles was extremely hazardous. The following is a list of types of goods, together with comments and suggestions, developed from available sources:

1. *Real and Personal Property and Equipment.* — Medical equipment supplies and the physician's residence (if this is included) may be appraised by real estate brokers, equipment dealers and other consultants in order to establish a fair market value. Most authorities felt that these constituted the basic, if not the only value, of a medical practice.

2. *Transferable Contract Appointments.*—If the seller holds appointments as an industrial consultant or house physician, or holds other positions providing a salary or other regular remuneration, the possibility of transferring these to the buyer may be explored. A value equal to an agreed percentage, perhaps of the annual income for the first year, may be established for this assured income.

3. *Lease of Office Space and Residence.*—While housing and office space continue to be in short supply in many parts of the country, a money value may be established for the transfer of leases on desirable space of this nature.

4. *Uncollected Bills.*—Bills for current services to patients or for relatively recent services may be transferred to the new physician for some consideration, or other arrangements for collections may be made which will be mutually agreeable. Often, the selling physician or his heirs will retain them for collection through their own agents.

5. *Goodwill.*—A formula or procedure has not been suggested which might be used consistently to establish a cash value for goodwill. One secretary commented, "I am of the personal opinion that it is absolutely impossible for a physician to set a price on goodwill or the value of a practice as such." Another stated, "It depends to a great extent on the value of services,

character and personality. One doctor may not be able to give the same services as the previous physician, or to pick up and use the goodwill left behind because of difference in personalities or other intangibles, and thus may lose all the goodwill." The general conclusion was that since the personal element is so important in the services provided by a physician, it may not be valid to assume that a physician's goodwill can be sold in the same fashion as a manufacturer's or a retail store's goodwill.

6. *Patients' Records.*—The problem of evaluating patients' records as to goodwill is even more difficult. Case histories, diagnostic reports, financial and other records can be of great value in assisting a new physician in the treatment of patients of the former physician. Many secretaries, however, felt that patients' records were essentially intangibles and therefore difficult to price. In addition, one secretary pointed out that ethical and legal issues are involved in transferring such records to a buyer without the patients' consent. To some extent this objection may be overcome if arrangements are made to have the buyer introduced to the community by the retiring physician as a professional associate for a period of time. Several secretaries felt that this is a more valuable arrangement in rural areas than in urban areas.

NO RULES OF THUMB

The buying physician may agree that the location, introduction to old patients or other circumstances will assure a steadier patient load than if he were to start a practice without these advantages. Basically, any inherent money value in these intangibles is reflected in the number of old patients who will continue to come to the buying physician. The buying physician may agree to pay the seller a given percentage of net income received from old patients during the first year or two; new patients during the first year may or may not be considered a separate or additional goodwill item. It should be clear to both parties that generalizations or "rules of thumb" regarding the probable percentage of old patients who will accept the new physician are open to serious question when applied to a given situation. Since prediction is so hazardous, both parties would be well advised to provide for final determinations of this item of goodwill a year or two later, although the formula may be set forth in the contract. This arrangement is considered also in cases in which a partnership or group is dissolved, but often it will involve much more complex formulas for establishing the interest of each member.

Careful consideration from the point of view of medical ethics should be given to any mutually satisfactory arrangement providing payments for the goodwill item out of future income or basing the value of this item on future income.

SPECIALTY PRACTICE

The question of sale or purchase of a specialty practice involves further difficulties. As a specialist depends greatly on referred patients, greater care must be taken to verify the continuation of a sound relationship with referring physicians. A general suggestion, both for a specialty practice and for a general practice, is to consider employment of a young man on a salary basis, with agreement as to terms of eventual sale or shift to partnership activity. In some instances such an agreement might prove more satisfactory to both parties than an outright sale.

CONCLUSIONS

The physician should exercise extreme care in arranging to sell or purchase a practice. Perhaps the best statement on the problem is the following by one of the state secretaries:

> The location, the type of practice, the size of the practice and the competition that is present are all factors which must be considered in each individual sale, and it appears that probably there is no formula that can be set up—even with an area such as a state—that would assist in any individual transaction. I am inclined to look on this as an individual business venture that would depend entirely on an agreement between the parties concerned. Even though in the eyes of every one else the purchase price was too high or too low, if it was agreeable to the two parties concerned, it would still be a happy transaction. And for those reasons, it has been the opinion of the society that it would not interfere or attempt to offer any assistance to persons contemplating the purchase of a practice.

Because of the extremely involved professional and financial interests arising out of such negotiations, the Bureau of Medical Economic Research strongly urges that principals make no final arrangements without the assistance of their attorneys. This is especially true if the transaction cannot be consummated at once but involves payments or professional relationships, such as partnerships, which extend over a period of time. Additional technical information and assistance on legal aspects of these contract matters is available to physicians' attorneys through the Association's Bureau of Legal Medicine and Legislation.

One alternative to the purchase of a practice was suggested by several secretaries—the establishment of a new practice in a community. If, after exploring the advantages and disadvantages of buying a given practice, it appears that there is no singular value in the location, type of practice or tangible goods, the physician can give serious consideration to the selection of another location in the community. It is this alternative which largely accounts for the infrequency of sales and the tenuous value of the goodwill item in medical practices in the United States.

Medical Legislation

STATE LEGISLATION

Massachusetts

Bills Introduced.—H. 89, to amend the medical practice act, proposes to authorize the board to accept the certificate of the national board of medical examiners or the certificate of the national board of examiners for **osteopathic physicians** and surgeons of the American Osteopathic Association, in place of its own professional examination, provided the applicant has not previously attempted unsuccessfully to secure registration in the state. H. 94, relating to the **fees of physicians,** proposes that a physician's fee for making an authorized mental and physical examination shall be $7 plus 20 cents for each mile traveled one way. H. 103, relating to the **physical examination of school children,** proposes that the board of health shall cause every child in the public schools to be separately and carefully examined at certain intervals to ascertain defects in sight or hearing and other physical defects tending to prevent his receiving the full benefit of his school work. The proposal also requires that a physical record of each child be kept in such form as the department of health may require. H. 934 proposes a resolution to the Congress of the United States memorializing the Congress to enact legislation providing for the establishment of a **National Science Foundation** with the appropriation of sufficient funds to encourage scientific research to be conducted which shall be made available to the directors of the armed forces and insure national security in the future. H. 978, to **amend the medical practice act,** proposes to authorize any person whose certificate has been suspended, revoked or canceled to file a bill in equity within ninety days for the purpose of reviewing such suspension, revocation or cancellation. H. 991, to **amend the workmen's compensation act,** proposes that the employee's physician's fee shall not be less than the highest fee which the insurer agreed to pay any physician who appears and testifies in its behalf. H. 999 and S. 231 propose the enactment of a Massachusetts **cash sickness compensation act.** H. 1069 to amend the law relating to the sale and **distribution of drugs and medicines,** proposes that no harmful drug shall be sold at retail or dispensed or given away to any person except on the written prescription of a physician, dentist or veterinarian and that no prescription for a hypnotic or somnifacient drug or any other harmful drug shall be renewed or refilled by a pharmacist if the prescription bears any indication that it is not to be renewed or refilled. **"Harmful drug" is then defined** by the proposal as including amidopyrine, "benzedrine," cantharides, cinchophen, digitalis, dinitrocresol, dinitrophenol, ergot, estrogen, natural or synthetic, barbituric acid, chloral hydrate, paraldehyde, sulfonamide drugs, thyroid, oil of croton, oil of pennyroyal, oil of savin and oil of tansy, and any other drug deemed by the department of public health or the board of registration in pharmacy to be a harmful drug. H. 1071 proposes that no licensed physician in the state shall be **discriminated against** or refused the right to practice his medical profession in any public hospital supported by public funds because said physician is not a member of a private medical society. H. 1074 and S. 348 propose to require **certain food handlers** to undergo regular physical examinations for tuberculosis or any other communicable disease which might endanger any person with whom he or she may come in contact. H. 1082 and H. 1638 propose to require any person who purchases or acquires a **dog, cat or bird** to be used for experimentation or mutilation while alive to keep a record and submit a report to the commission of public safety of each such transaction showing the source from which such animal or bird was obtained. H. 1090 proposes to prohibit the **vivisection** of any living dog within the commonwealth of Massachusetts. H. 1097 and S. 264 propose to prohibit any person from **experimenting on living animals** without a license from the state board of registration in veterinary medicine. Surgical experiments on such animals are permitted in certain specified circumstances. H. 1280, to amend the workmen's compensation law, proposes that the **reasonable cost of a physician's service** shall include a routine laboratory service fee for such service which should be allowed to every patient in order to diagnose honestly his injury, his condition and the effect of such condition on the injury. The reasonable cost of a physician's services would also include laboratory fees, x-ray fees and court witness fees

for the time which the physician spent in court. H. 1463 proposes the creation of a Massachusetts **cash sickness compensation fund.** H. 1526 proposes to repeal all existing laws requiring **vaccination.** S. 230 proposes the enactment of a nonoccupational accident and **sickness benefits law.** S. 252 proposes the creation of a board of registration of **chiropractors** and defines chiropractic as "the science of locating and removing, by hand adjustment only, interference with the transmission or expression of nerve force in the human body, by the correction of misalignment of subluxations of the vertebral column. It excludes operative surgery, prescription or use of drugs or medicine, or the practice of obstetrics, except that the x-ray may be used solely for the purposes of examinations; chiropractor is defined as a person who lawfully practices chiropractic."

Mississippi

Bills Introduced.—H. 24 proposes an appropriation to the state building commission for the purpose of erecting and equipping necessary buildings for a fully accredited Grade A **four-year medical college,** as a department of the University of Mississippi. H. 43 proposes the enactment of a Mississippi Workmen's **Compensation Act.**

New York

Bills Introduced.—A. 143 and S. 139 propose to repeal the existing law requiring persons, firms or corporations engaged in the business of procuring persons as **blood donors** to be licensed by the local health officer and requiring blood donors to present a certificate from a physician showing satisfactory physical condition before making the blood donation. A. 187, A. 275, S. 287, S. 301 and S. 371, to **amend the unemployment compensation law,** propose to authorize the payment of benefits to persons unemployed because of illness or disability, where such illness or disability is certified by a physician or surgeon duly licensed to practice in the state of New York. A. 362 proposes to regulate the working hours of **registered professional nurses.** A. 409, S. 285 and S. 410, to amend the **unemployment insurance law,** propose to extend the benefits thereof to persons employed by charitable and nonprofit institutions.

Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 9-10. Dr. Donald G. Anderson, 535 North Dearborn St., Chicago 10, Secretary.

National Conference on Rural Health, Chicago, Palmer House, Feb. 6-7. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

American College of Allergists, New York, Hotel Pennsylvania, March 12-14. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Philadelphia, Feb. 26. Dr. Norman N. Smith, 291 Whitney Ave., New Haven 11, Conn., Secretary.

American Society of Biological Chemists, Atlantic City, March 14-19. Dr. Otto A. Bessey, Public Health Research Institute, New York 19, Secretary.

Central Surgical Association, Chicago, Drake Hotel, Feb. 19-21. Dr. Walter G. Maddock, 250 E. Superior St., Chicago 11, Secretary.

Chicago Medical Society Annual Clinical Conference, Chicago, Palmer House, March 2-5. Dr. Willard O. Thompson, 30 N. Michigan Blvd., Chicago 2, Secretary.

Dallas Southern Clinical Society, Dallas, Texas, Hotel Adolphus, March 15-18. Dr. Glenn D. Carlson, 1133 Medical Arts Bldg., Dallas, Secretary.

Michigan Postgraduate Clinical Conference, Detroit, Book-Cadillac Hotel, March 10-12. Dr. H. H. Cummings, 2014 Olds Tower, Lansing 8, Chairman.

Mid-South Postgraduate Medical Assembly, Memphis, Tenn., Feb. 10-13. Dr. Arthur F. Cooper, 1479 Carr Ave., Memphis, Secretary.

Missouri State Medical Association, St. Louis, Hotel Jefferson, March 14-17. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Exec. Secretary.

National Conference on Medical Service, Chicago, Palmer House, Feb. 8. Dr. Edward F. Sladek, 232 E. Front St., Traverse City, Mich., Secretary.

New Orleans Graduate Medical Assembly, New Orleans, Municipal Auditorium, Feb. 23-26. Dr. Max M. Green, 1430 Tulane Ave., Room 105, New Orleans 13, Secretary.

Pacific Coast Surgical Association, Los Angeles, Ambassador Hotel, Feb. 24-28. Dr. Carleton Mathewson Jr., Stanford Univ. Hospital, San Francisco, Secretary.

Tri-States Medical Association of the Carolinas and Virginia, Charleston, S. C., Fort Sumter Hotel, Feb. 9-10. Dr. James M. Northington, 306 N. Tryon St., Charlotte 2, Secretary.

United States-Mexico Border Public Health Association, Laredo, Texas and Nueva Laredo, Mexico, March 20-22. Dr. M. F. Haralson, U. S. Court House, El Paso, Texas, Secretary.

Washington Letter

(From a Special Correspondent)

Jan. 29, 1947.

Taft Says Administration Health Bill Would Nationalize Medicine

In answer to a query following his address to the American Public Relations Association, Senator Robert A. Taft of Ohio, chairman of the Senate Republican steering committee, charged that the Wagner-Murray-Dingell bill would "not only socialize medicine but would nationalize medicine." He declared that the measure would actually provide some $5,000,000,000 in revenue to Washington bureaus to distribute for free medical aid. The Taft-Smith-Ball-Donnell bill, on the other hand, would give free medical care only to those who cannot afford it. Speaking in general of his proposed health, welfare, housing and educational program, Senator Taft said: "I have a strong feeling that in this country if we have a large enough production we can try to abolish hardship and poverty. Whether through their own misfortune or not, there always seems to be a group that is bound to be behind. I think that the other 80 per cent of the people can try to bring them up to a reasonable standard of living in health, housing and education."

Reports Veterans' Medicine Suffers from Lack of Funds

Dr. Paul B. Magnuson, medical director of the Veterans Administration, declared that medical activities of the agency are being held down "all along the line" to stay within budgetary limits. Recently the Disabled American Veterans informed members of Congress of the financial plight of the veterans' medical program when they recommended a $32,000,000 deficiency appropriation. Dr. Magnuson said that he does not expect to ask Congress for such an appropriation at this time, but he has urged that steps be taken so that there will be no repetition of the current situation. He reported that the hospital program will meet difficult times in four months when about 1,400 young military physicians assigned to the agency—those trained through the AST and the Navy V-12 programs, become eligible for release from the service. Great difficulty is now being experienced in the outpatient service, where officials claim that the number of applications for treatment are far in excess of such requests a year ago. Dr. Magnuson reported that approximately 500,000 veterans are awaiting dental treatment and about 70,000 others are awaiting examinations for outpatient medical care. Dr. Magnuson informed a press conference that he is preparing for the American Medical Association a list of the names of physicians suspected of "chiseling" on "fee basis" treatment for veterans, under the program whereby the government reimburses physicians for treatment given. Dr. E. M. Kennedy of the Veterans Administration dental service said that dental costs are taking some 70 per cent of the amount set aside for outpatient care. The medical budget for the current year totals $452,000,000, of which $210,000,000 is for salaries of all personnel. Salaries of Veterans Administration doctors and dentists total $40,000,000. Of the remaining $242,000,000, the sum of $77,000,000 is for outpatient medical and dental programs.

Delay in Ratifying World Health Organization Note

The *Washington Post* commented editorially on the delay in ratifying the World Health Organization's constitution by all twenty-six members of the United Nations. To date seventeen nations have ratified, but Soviet Russia and the United States are among those that have not done so. When final ratification is obtained, the first World Health Assembly will be held within six months and the World Health Organization will become a full fledged member of the U. N. family. The *Post* commented: "Congress has, indeed, approved in principle, with some minor reservations, but the ratification bill was lost in the rush of the closing days of the last regular session of Congress. However, W. H. O. has not been inactive. Its work is being carried on by an Interim Commission, on which the United States is represented, the commission having its headquarters in New York and its technical office in Geneva, Switzerland. . . . Health problems are universal and are readily understood by even the simplest minds. Here is one international activity on which mankind should be able to unite."

GOVERNMENT SERVICES

NAVY

ONE YEAR EXPEDITION TO AFRICA

The Naval Medical Unit of the University of California's African Expedition sailed for Egypt January 14 to begin a year's research aimed to implement the prevention and cure of tropical diseases. Heading the naval unit is Comdr. J. M. Amberson (MC), U.S.N.; others in the unit are Comdr. T. K. Ruebush (MSC), parasitologist; E. Schwarz, zoologist; Chief Pharmacist Mate D. K. Lawless, parasitology technician, and Photographers Mate (second class) Harley S. Cope Jr., all of the Naval Medical School, as well as Mr. Harry Hoogstrall, entomologist, of the Field Museum, Chicago. The expedition will leave Alexandria, Egypt, early in February and will follow a southerly course through Central Africa to the Cape of Good Hope. The itinerary of the trip has been based on months of research and planning. Emphasis will be placed on making surveys and collections in certain areas. The safari will go through the Nubian Desert and will explore an area in which major collections were last made in 1830 by Ruppell, Hemprich and Ehrenberg. Collections will also be made in the Nuba Mountains and in the Jezira triangle, between the White and Blue Nile rivers.

From April to July Nairobi will be headquarters for a survey of Nenya, Uganda, the eastern Belgian Congo and, tentatively, Abyssinian Somaliland. During the wet months work will be done in the northern and northeastern areas, to include Lake Rudolf, the coastal country toward Somaliland, Pemba and Zanzibar Islands, and Central Tanganyika. Uganda, the Belgian Congo and the high mountains will have to be surveyed late in May and June.

While in the Union of South Africa the medical group will gather evidence relating to the effect of industrialization on the health condition of the African Negro. The shift of population from the tropics to the settled southern area will be considered.

The naval group will attempt to make a representative collection of South African flora and fauna for American institutions. The medical unit will seek material to be used for teaching purposes at the Naval Medical School, Bethesda, Md. Anatomic and pathologic specimens, blood smears, protozoa and bacteria, vectors of parasites, intermediate hosts and vertebrates, as well as live specimens to be used as laboratory animals, and pertinent photographic records will comprise part of the documentary evidence to be procured. New drugs and chemicals will be tested for control of infections, parasites and pests, and cooperation with local health authorities and research institutions will be sought.

MEETING OF RESERVE CONSULTANTS

The Reserve Consultants Board to the Bureau of Medicine and Surgery, Navy Department, held its annual meeting at the National Naval Medical Center, Bethesda, Md., on January 9. Dr. Winchell M. Craig, Rochester, Minn., is chairman of the board, which consists of former members of the Medical Department of the Navy. The agenda was comprised chiefly of items relating to the graduate training program of the Naval Medical Department. The amount of training to be given, the eligibility requirements for graduate training and the location of such training facilities were topics under discussion. The group was addressed by Rear Admiral Clifford A. Swanson, Surgeon General of the Navy.

MISCELLANEOUS

NEW COMMITTEE ON ISOTOPE DISTRIBUTION

The Atomic Energy Commission has appointed a new Advisory Committee on Isotope Distribution. This group will recommend to the commission new policies governing the distribution of isotopes, will review existing policies and will act as adviser to the Isotopes Division of the Atomic Energy Commission on allocation of isotopic materials. G. Failla, Columbia University Medical School, New York, is chairman of the new committee; other members are Hymer L. Friedell, Western Reserve University, Cleveland; A. H. Holland Jr., medical adviser, Oak Ridge, Tenn.; J. G. Hamilton, University of California; Joseph W. Kennedy, Washington University, St. Louis; Robley D. Evans, Massachusetts Institute of Technology; Robert F. Mehl, Carnegie Institute of Technology; Austin M. Brues, Argonne National Laboratory, Chicago; L. N. Nims, Brookhaven National Laboratory, Upton, Long Island, N. Y.; H. A. Barker, University of California, Berkeley; Henry Borsook, California Institute of Technology, Pasadena, and Paul C. Aebersold, Oak Ridge, Tenn.

A Subcommittee on Human Applications will consist of Drs. Failla, Friedell, Hamilton and Holland. Membership of a Subcommittee on Allocation will be Drs. Kennedy, Nims, Mehl, Brues, Evans, Barker and Borsook. Dr. Aebersold will serve as secretary to the committee and its subcommittees and as liaison representative of the Atomic Energy Commission.

The new committee held its first meeting in Washington, D. C., January 20. The Atomic Energy Commission has accepted with regret the resignation, effective Dec. 31, 1947, of the Interim Advisory Committee on Isotope Distribution Policy and of its two subcommittees, on human applications and on allocation. The interim committee and its subcommittees were appointed by Major Gen. L. R. Groves of the Manhattan Project. They recommended the general policies on which the Manhattan District initiated its radioisotope distribution program and under which the commission has continued this activity. The subcommittees assisted the Isotopes Division at Oak Ridge in the review and evaluation of requests for radioactive isotopes and made recommendations on allocations of such materials.

LABORATORY RECEIVES DISTINGUISHED SERVICE AWARD

The laboratory of the Bureau of Entomology and Plant Quarantine at Orlando, Fla., has been awarded the Distinguished Service Award by the U. S. Department of Agriculture "for the development and application of means of protecting military personnel against attack by insects and diseases spread by insects." At the ceremony at the laboratory, January 24, the award was presented by the assistant secretary of agriculture, Mr. Charles F. Brannon. The research which the laboratory conducted during the war on these problems was sponsored by the Army and the Navy and made possible by the transfer of funds to the Department of Agriculture by the Office of Scientific Research and Development. During the afternoon of January 24 the laboratory held open house to enable visitors to see the laboratory and discuss the activities now under way on various arthropods that attack man.

SALE OF SURPLUS GOVERNMENT PROPERTY

The War Assets Administration announces a sale of miscellaneous drugs and medical supplies from January 27 to February 16. Sales will be made through War Assets Administration customer service centers which are located in numerous large cities throughout the country. Veterans have certain priorities with respect to the sale. Orders sent to any customer service center must be received on or before February 16.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Butler, Charles L.....New Hope
Kelly, Alexander P. Jr.....Camp Rucker
Moody, Marcus D.....Childersburg
Thames, Arnold F.....Mobile

Arkansas

Easterling, Thomas G.....Chicot
Harper, Edwin O.....Arkadelphia
Harris, Julian L.....Hazen
Hinkle, Richard A.....Conway
Parkerson, Cecil W.....Little Rock

California

Bonoff, Chester P.....Los Angeles
Borden, David G.....Berkeley
Greenberg, Albert K.....San Francisco
Hanson, Elmer F.....Burlingame
Jung, Edmund D.....San Francisco
Lawson, William R.....Pasadena
Lenert, Charles.....Oakland
Mann, Leslie B. Jr.....Los Angeles
Murphy, John C.....San Diego
Rector, Elijah W.....Nevada City
Salin, Rolfe W.....Redwood City
Strong, Edward K...Stanford University
Sutherland, Walter H.....Los Angeles
Williams, Ernest L.....Inglewood
Woodward, Stanley R.....Los Angeles

Colorado

Kerr, Richard C.....Boulder
Waddell, Emmett P.....Denver

Connecticut

Almklov, John R.....New Haven
Jones, James F.....Danielson
Serena, Frank A.....South Norwalk
Stein, Julius D.....Milford

District of Columbia

Cross, Louis L Jr.....Washington
Daines, Joseph G.....Washington
Litvin, Philip.....Washington
McLeod, Robert N. Jr.....Washington
Taylor, Robert G.....Washington

Florida

Anderson, George H.....St. Petersburg
Ganey, Joseph B.....Bradenton
Price, Morris A.....St. Augustine
Rogero, Clarence R. Jr.....St. Augustine
Summerlin, Glenn O.....Gainesville

Georgia

Guy, John C.....Atlanta
Marks, Edward S.....Toccoa
Moon, Jack B.....Augusta
O'Neal, John B. III.....Waycross
Russell, David A. Jr.....Atlanta

Illinois

Barnes, Benjamin A.....Chicago
Chickering, William A.....Chicago
Christian, Joseph R.....Oak Park
Ewart, Fred E. Jr.....Oak Park
Joslyn, Howard P.....Oak Park
Killian, Edgar W.....Chicago
King, Thomas J.....Chicago
Kinney, Edward J.....Dixon
Levett, Harry L.....Chicago
Lininger, Richard E.....Evanston
Murphy, Robert H.....Joliet
Nemecek, Joseph G.....Chicago
Pfeiffenberger, Mather.....Alton
Rosenman, Ray H.....Chicago
Roth, Julius A.....Carlinville
Schreider, Jonas E.....Chicago
Stanon, Roy F. Jr.....St. Louis
Tucker, Sheldon M.....Chicago

Maine

Melendy, Oakley A.....Gardiner

Maryland

Byrne, Robert F.....Silver Spring
Davis, Marvin H.....Baltimore
Guyther, Joseph R.....Mechanicsville
Karzon, David T.....Baltimore
Myers, Joseph C.....Woodlawn
Myers, Myron J.....Baltimore
Ullsperger, John F.....Baltimore

Massachusetts

Crawford, John D.....Cambridge
Gardella, Joseph W.....Arlington
Harris, John W.....Boston
Hoff, Irving.....Holyoke
Lynch, Joseph P. Jr.....Marlboro
Murray, Joseph E.....Milford
Rizzo, Nicholas D.....Brighton
Schlessinger, Paul J. R...South Attleboro
Whittlesey, Philip.....Newton Center

Michigan

Barone, Charles G.....Highland Park
Castle, Maurice E.....Detroit
Clark, Charles E.....Detroit
Dehlin, James R.....Gladstone
Hallen, Leonard J.....Detroit
Ray, Dean K.....Gobels
Stewart, Lewis L.....Detroit
Torrey, Francis A.....Lake City

Minnesota

Freeman, John G.....St. Peter
Helmsworth, James A....N. Minneapolis
Hitchcock, Claude R.....Minneapolis
Jones, David G.....Minneapolis
Larson, Paul G.....Montevideo
Litman, Robert E.....Minneapolis
Rotnem, Orville M.....Minneapolis
Salkin, Murray R.....Minneapolis
Sandeno, Morris T.....Kenyon
Schultz, Donald O.....Moose Lake
Wolgamot, John R.....Albert Lea

Missouri

Goldfarb, Alvin.....St. Louis
Hughes, Gerald E. III.....Kansas City
Jones, Max P.....Stanberry
Joyce, Gerald B.....Kansas City
Klingberg, William G.....St. Louis
Macfarlane, Lloyd W.....St. Louis
Mills, Warren B.....Webster Groves
Moore, Andrew M.....St. Louis
Sudholt, Alfred Felix Jr.....St. Louis
Vivona, Stefano.....St. Louis

Montana

Quinn, James W.....Missoula
Wessell, Maurice S.....Hamilton

Nebraska

Bleicher, Jerome E.....Omaha
Gately, Harold S.....Syracuse
Kratochvil, Charles M.....Omaha
Nelson, Wallace W.....Albion
Olson, Leland J.....Palmyra
Snyder, John T.....Nemaha

New Hampshire

Hinkley, Robert I.....Lancaster
Nemiah, John C.....Hanover

New Jersey

Goldstein, Joseph R.....Atlantic City
Greif, Jacob L.....New Brunswick
Kemezis, Vita J.....Kearney
Kosovsky, Harry.....Passaic
Levitzky, Edward.....Rahway
London, Robert D.....Perth Amboy
Orloff, Jack.....Newark
Otvos, Emery G.....Palisade
Perkel, Harold.....Jersey City
Willner, Albert.....Newark

New Mexico

Smith, Jacques M.....Las Vegas

New York

Bien, Edward J.....Mastic Beach
Capers, Ellison V.....Poughkeepsie
Coren, Adrian R.....Brooklyn
Fleischman, Henry.....Astoria, L. I.
Flynn, Frederick J. Jr.....Jamaica
Friend, John W.....Brooklyn
Gelfand, Daniel E.....Bronx
Gemson, Bennett L.....Brooklyn
Green, Robert E.....Yonkers
Greene, Richard W.....Binghamton
Greenfield, Gerald.....Brooklyn
Hagen, Samuel J.....Buffalo
Hartnett, Bernard J.....Moravia
Hood, Robert I.....Corning
Izzo, Gerard N.....Brooklyn
Kelter, Joseph J.....Brooklyn
Koenig, Leonard J.....Ozone Park
Lasser, Richard P.....Brooklyn
Ling, Alexander.....Floral Park, L. I.
Lowenthal, Martin.....Brooklyn
Lundgren, Lawrence E.....Plattsburg
Mazzeo, Vincent P.....Brooklyn
Mond, Irving.....Brooklyn
Montross, Henry E.....New York
Osborn, John J.....Garrison-on-Hudson
Pender, Robert B.....Utica
Pisciotta, Anthony V.....New York
Porrazzo, Andrew P.....Brooklyn
Rechtschaffen, Joseph S.....Brooklyn
Rigney, Thomas G.....Elmurst, L. I.
Ross, Jack F.....Lockport
Rubin, Tobias M.....Yonkers
Russo, Vincent.....Franklin Square
Schmatolia, Ernest.....New York
Schneck, Jerome M.....Forest Hills
Semenoff, Louis.....Catskill
Singiser, James A.....Mount Kisco
Sneid, Philip.....New York
Stannard, Edson L.....Port Washington
Sternberg, Stephen S.....New York
Susselman, Samuel.....Albany
Tripp, Samuel E.....Oswego
Turner, Louis B.....New York
Utell, Milton C.....New York
Walsh, Ambrose G.....Liverpool
West, Byron S.....Sherburne
Wolleben, John E.....Brooklyn

Oregon

Banfield, Ernest E. Jr.....Portland
Bell, Max F.....Portland
Burget, William M.....Portland
Condon, Robert J.....Portland
Cottel, Charles E.....Portland
Holm, Carl L.....Silverton
Lowell, Roy S.....Portland
Merriss, Martin D.....Portland
O'Connor, Owen J.....Clackamas
Page, Lucius K.....Portland
Radding, Jerome.....Portland
Todd, Jerry H.....Portland

Texas

Bettis, Moody C.....Brownwood
Branch, William M. Jr.....El Paso
Brooks, Thomas C.....Waco
Childers, Herschel N.....San Antonio
Evans, Ward.....El Paso
Haley, Raphael R.....Dallas
Kallina, Frederick P.....Garwood
Lang, Garland H. Jr.....Kerrville
McClelland, Gene A.....Gilmer
Smallberg, William A. Jr.....El Paso
Zatopek, Leland F.....Columbus

Canada

Lukens, Theodore J.....Oshawa, Ont.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

COLORADO

University Appointments.—Dr. Frank Princi, Denver, has been appointed director of the division of industrial medicine and assistant professor of medicine at the University of Colorado Medical Center. Dr. Princi is a graduate of the University of Colorado School of Medicine.

Dr. Stuart G. Smith, Washington, D. C., has joined the medical center staff to teach in the department of anatomy. Dr. Smith is a graduate of Western Reserve Medical School, Cleveland.

Open Ward for Tuberculous Patients.—A new ward for the care of patients with tuberculosis will be opened at Colorado General Hospital, Denver, about February 1 through alterations of a ward used for the care of patients with poliomyelitis for the past year and a half. About twenty-eight patients can be accommodated, priority being given to those requiring surgical operation. Provision for the ward was made by the legislature as the first step to be taken by the state for hospital care of tuberculous patients. Selection of the staff is being made. The director of nursing at Colorado General Hospital is particularly desirous of hearing from nurses and attendants interested in working in this field.

CONNECTICUT

Cancer Conference.—Connecticut's first cancer conference for physicians will be held at the Hotel Taft, New Haven, Thursday, March 25. The conference is being arranged by the Connecticut Cancer Society with the cooperation of the state medical society. The program will present well known national speakers who will discuss cancer with special emphasis on early detection by family physicians and the means available for early treatment.

Appointed to Examining Board.—Dr. Louis P. Hastings, West Hartford, was recently appointed to the Connecticut Medical Examining Board to succeed Dr. Charles J. Bartlett, New Haven, resigned. Dr. Hastings is president of the Hartford County Medical Association and has been on the full time staff of St. Francis Hospital, Hartford, since 1929. Dr. Bartlett was president of the board at the time of his resignation, and his membership was continuous for more than twenty years. He was appointed professor of pathology at Yale University School of Medicine in 1897 and was named professor emeritus in 1917. He has been pathologist at the Grace-New Haven Community Hospital since 1918.

ILLINOIS

Report on Communicable Diseases.—The Illinois state health department reports that about 12 in each thousand of the state's population suffered an attack of one or another of the notifiable diseases during 1947. In the previous year the rate was 16 per thousand. Venereal diseases were responsible for almost half of all cases reported, although figures are below those for venereal disease reported for 1946. Smallpox and scarlet fever fell to the lowest reported incidence on record in the state; diphtheria case reports totaled 174 as compared with 469 for 1946; tuberculosis increased to 7,915 cases as against 7,431 in 1946, an increase attributed to "effective case-finding efforts"; and typhoid accounted for 137 cases as against 106 for 1946.

Chicago

Research on Amino Acid Therapy.—The Hektoen Institute for Medical Research at Cook County Hospital has received its annual grant of $25,000 from the Biochemical Division of the Interchemical Corporation. This grant is to support research on intravenous amino acid therapy and on the role of individual amino acids in human metabolism. One objective of the research program to be pursued is the formulation of an amino acid mixture to be given by vein that will best satisfy physiologic requirements for nitrogen balance.

Fellowship in Allergy.—The Division of Allergy, Northwestern University Medical School, announces a fellowship for training in allergy. Candidates should have experience in research or in basic sciences. The fellow will receive training in clinical allergy and in research and may register for an M.S. degree. The stipend is $1,800 to $3,000. Similar training, without stipend, is also offered to a candidate whose qualifications do not meet fellowship requirements. For information address Dr. Samuel M. Feinberg, Northwestern University Medical School, Chicago.

Society News.—The North Side Branch Chicago Medical Society will be addressed by the following speakers February 5 in the Drake Hotel at 8 p.m.:

Dr. George F. Lull, Secretary and General Manager of the American Medical Association, Chicago, The American Medical Association and Its Relation to the Public.

Dr. Benjamin M. Baker Jr., Johns Hopkins University, Baltimore, Clinical Aspects of Some Diseases of Collagen Degeneration.

Dr. William F. Rienhoff Jr., Johns Hopkins University, Baltimore, Surgical Treatment of Hyperparathyroidism.

The scientific program will be preceded with a fellowship gathering at 5:30 and dinner at 6:30 p.m. Reservations are required.

This Week in Chicago Medicine.—The Chicago Medical Society has inaugurated a weekly mimeographed publication entitled *This Week in Chicago Medicine,* designed to keep the profession posted and to aid out of town physicians who wish to visit clinics, conferences, round tables or other meetings. The society is sending copies to all medical libraries, medical schools and city medical societies in the country; to all Illinois hospitals and hospitals of larger cities in states adjacent to Illinois. Loop hotels have requested copies to give to guests who are physicians. Any doctor planning a trip to Chicago may secure copies of this bulletin by writing to the Chicago Medical Society, 30 North Michigan Avenue, Chicago.

KENTUCKY

Society of Anesthesiology.—The newly organized Kentucky Society of Anesthesiology met in Louisville December 3 and elected Dr. Samuel S. Clark, Louisville, president; Dr. Joseph S. Parker, secretary, and Dr. German P. Dillon Jr., treasurer. The society, which has twenty-eight charter members, will meet once a month in the interest of progress and research in anesthesiology.

MICHIGAN

Postgraduate Courses at Wayne.—Wayne University College of Medicine, Detroit, is offering a full time course in basic ophthalmology from January 15 to June 15. Enrolment in the course is limited to twenty. The fee is $300. The college is also offering a postgraduate course in the basic sciences from March 15 to June 12.

Appointments to State Board.—Three new appointments to the State Board of Registration in Medicine, subject to senate approval, are Drs. Cyrus B. Gardner Lansing; Leland E. Holly, Muskegon, and Cecil Corley, Jackson. Reappointed for the four year term are Drs. David C. Eisele, Ironwood, and Franklin V. Troost, Holt.

MINNESOTA

Personal.—Dr. Fred W. Wittich, Minneapolis, has been notified by the state department that he has been awarded a diploma for allergy lectures delivered at the Instituto Brasileiro de Historia in Rio de Janeiro, Brazil, in December 1946.

Gift of Annual Lectureship.—The Minnesota Graduate Club and Alpha Xi Undergraduate Chapter of the Phi Delta Epsilon fraternity will present an annual lectureship to the University of Minnesota Medical School, Minneapolis, at a banquet February 26. The first lecture will be given after the banquet in the Medical Sciences Amphitheater of the university by Dr. William Roemmich, Oak Terrace, U. S. Public Health Service, on "The 1947 Chest X-Ray Survey of Hennepin County."

NEBRASKA

Society Election.—The Omaha Mid-West Clinical Society has elected the following Omaha physicians as officers for 1948: Roy W. Fouts, president; Warren Thompson, president-elect; John M. Thomas, secretary and director of clinics, and Louis E. Moon, treasurer. October 25 to 29 are the dates for the 1948 meeting.

University Appointments.—Recent appointments to the faculty of Creighton University School of Medicine, Omaha, include Dr. A. S. Black Jr., asisstant in surgery (plastic surgery); Dr. C. F. Lowry, assistant in medicine; D. M. C. Reilly, Ph.D., instructor in biochemistry, and J. M. Severens, Ph.D., assistant professor of bacteriology.

Dr. Bennett Leaves for California.—Dr. Abram E. Bennett, for many years chairman of the department of neuropsychiatry at the University of Nebraska College of Medicine, Omaha, will become affiliated with the Herrick Memorial Hospital, Berkeley, Calif., on March 1. The hospital is opening a new forty bed psychiatric department.

NEW YORK

Ordinance on Atmospheric Pollution.—Niagara Falls is the first city in the United States to adopt an ordinance providing complete coverage for all types of atmospheric pollution —dusts, gases, fumes, mists, vapors, smoke and odors. The ordinance is also unique in setting up an air pollution control board to keep rules flexible. The U. S. Public Health Service, Industrial Hygiene Division, assisted in this project at the request of the city and state.

Professional Recruitment and Training.—Dr. Franklyn B. Amos, Delmar, has been appointed director of the state health department's new office of professional recruitment and training, effective January 1. He will supervise programs to train physicians, nurses, engineers, dentists and health educators for public health work. Dr. Amos, a graduate of Syracuse University College of Medicine, 1931, has been with the state health department since 1935 and has been director of local health administration since 1940.

Centennial of Community Service.—The Community Service Society is celebrating its centennial year with a series of scientific conferences, bringing together leaders in the fields of medicine, psychiatry, the social sciences, public health and education beginning January 22 and continuing through April. The theme is "The Family in Tomorrow's World." Dr. Thomas M. French, Chicago, spoke on "Personal Interaction and Growth in Family Life" at the first of three symposiums at the Hotel Roosevelt on January 29. On January 30 Dr. Marianne Kris, New York, spoke on "Implications (of Child Rearing) for Family and Community"; Dr. Nathan W. Ackerman, New York, on "Adaptive Problems of the Adolescent Personality," and Dr. Viola Bernard, New York, "Implications (of Adolescence) for Family and Community."

The Community Service Society is said to be the largest private nonsectarian family and health agency in the United States. It is the modern outgrowth of two pioneer organizations, the Association for Improving the Condition of the Poor, incorporated in 1848, and the Charity Organization Society, founded in 1882.

New York City

Strausberg Memorial Lecture.—The first Samuel Strausberg Memorial Lecture of the Beth-El Hospital, Brooklyn, will be delivered by Dr. William Goldring, associate professor of medicine at the New York University College of Medicine, February 18 in the Kings County Medical Society building. Dr. Goldring's topic will be "Present Status of Medical and Surgical Treatment of Hypertension." The lecture is in memory of the late Mr. Strausberg, president of the hospital, 1941 to 1946.

Research on Problems of Aging.—Columbia University, New York, has been awarded a grant of $31,500 by the Rockefeller Foundation for "investigation of the interaction of hereditary and environmental factors in relation to the problems of aging." The grant, a renewal of an original gift made by the foundation in 1945 to the New York State Psychiatric Institute, a part of the Columbia-Presbyterian Medical Center, will carry on a three year or longer investigation on the health status and activities of twins over 60 years of age. A number of state and private agencies are cooperating. There is still a need for twins of more than 60 years of age in New York City to participate in the study. Those interested are asked to communicate with the Department of Psychiatry, 722 West 168th Street, New York 32.

NORTH CAROLINA

Narcotic Violation.—The Bureau of Narcotics, Washington, D. C., reports that Dr. Wiley R. Young, Angier, N. C., pleaded guilty to violation of the federal narcotic law in the U. S. District Court at Greensboro on Dec. 2, 1947. His sentence of three years was suspended; he was placed on probation for a period of five years and was fined $500.

UTAH

Utah Medical Foundation Lecture.—Dr. Edith L. Potter, Chicago, will deliver the second series of the annual Obstetric and Gynecological Lectureship on "Immunization to the Rh Factor" and "Etiology of Maldevelopment of the Human Fetus" at the University of Utah, Salt Lake City, February 16 and 17.

WEST VIRGINIA

First Woman to Head Component Society.—Dr. S. Elizabeth McFetridge, Shepherdstown, has been elected president of the Eastern Panhandle Medical Society, the first woman to be named president of a component society of the West Virginia State Medical Association. In addition to her specialty of anesthesiology, Dr. McFetridge is engaged in general practice. She was recently named chairman of the association's Committee on Maternal Welfare.

Hunter Memorial Library.—Plans have been approved for establishing the Hunter Library at the Herbert J. Thomas Memorial Hospital, South Charleston, in memory of Dr. J. Ross Hunter, Charleston, who was president of the staff at the time of his death on Dec. 31, 1947. Contributions are being accepted by Mr. T. W. Patterson, hospital administrator. The long-range plan will probably include a circulating library for patients as well as the medical library proposed for the use of the staff.

Licensure to Practice.—Under a new regulation of the public health council a qualified applicant for licensure to practice medicine in West Virginia will hereafter be permitted to practice in a specified area during the interim between the filing of his application and the date of the next regular meeting of the public health council, at which time he will be required to appear for examination. Graduates of unclassified foreign medical schools will be permitted to serve as interns or residents in private hospitals and state institutions, provided their services are requested by the proper officials prior to employment and provided that they present their credentials to the public health council in regular session and receive permission so to serve. However, they will not be permitted to serve outside the hospitals or institutions. This regulation does not in any way rescind a previous regulation of the council, which bars graduates of Class B schools from practice in hospitals in this state after July 1, 1948.

GENERAL

Director of Information.—Joseph Hirsh, New York, associate director, Research Council on Problems of Alcohol, has been granted a leave of absence to assume the position of director of public information, World Health Organization, Interim Commission, of the United Nations. He participated in the fifth session of the World Health Organization, Interim Commission, in Geneva, Switzerland, January 1948.

Appoint Director of Public Health Nursing.—Miss Anna Fillmore, R.N., New York, has been appointed general director of the National Organization for Public Health Nursing to succeed Miss Ruth Houlton, R.N. Miss Fillmore has been with the Visiting Nurse Service of New York since 1940. Previously she was director of the Bureau of Public Health Nursing in the Utah State Health Department and assistant director of the American Nurses Association of New York.

Dr. Talbott to Edit *Medicine*.—Dr. John H. Talbott, professor of medicine, University of Buffalo Medical School, and head of the department of medicine, Buffalo General Hospital, has succeeded Dr. Alan M. Chesney, Baltimore, as managing editor of *Medicine*. Dr. Talbott received the M.D. degree from Harvard Medical School in 1929, and from 1931 to 1946 was associated with that school and the Massachusetts General Hospital in various capacities, being associate in medicine from 1935 to 1946.

National Foundation's Decade of Progress.—Basil O'Connor, head of the National Foundation for Infantile Paralysis, has reported that the organization in its first decade has spent $35,000,000 in medical care for victims of poliomyelitis and $13,000,000 for research on the disease. It has helped 88,000 patients financially, obtained admission for patients in four hundred and seventeen hospitals, started five hundred and forty research and education projects and trained thirteen hundred professional workers in the treatment of patients with poliomyelitis.

American Physicians Exhibit Art in Argentina.—On invitation from the Argentine government (THE JOURNAL, Sept. 20, 1947, p. 172) twenty-two physicians of the American Physicians Art Association submitted pieces in an exhibit of fine arts in Buenos Aires Nov. 24, 1947. Gold medals were awarded to Dr. Max Thorek, Chicago, and Dr. Homer Wheelon, Seattle, Wash. The art pieces were shipped prepaid by air freight through the courtesy of Mead Johnson & Company. Members of the American Physicians Art Association and the American Physicians Literary Guild have been invited to exhibit again at the next art show. A return invitation has been extended for the artists and literary physicians of Buenos Aires to exhibit in Chicago next June.

Lynch Memorial Essay Contest.—The Pacific Coast Obstetrical and Gynecological Society will hold its second Frank W. Lynch Memorial Essay Contest during the coming year. It is open to physicians who have been in practice for less than ten years or who have not been certified by the American Board of Obstetrics and Gynecology, Inc. Any topic may be selected in the obstetric or gynecologic field and may cover either clinical investigations or laboratory research. The prize for the best essay submitted is $100, and the winner will present his paper at the fall meeting of the society. Essays should be in the hands of the secretary, Dr. R. Glenn Craig, 490 Post Street, San Francisco 2, by August 1. Dr. Frank Lynch was first president of the society.

Conference for Children with Orthopedic Defects.—The National Foundation for Infantile Paralysis is sponsoring a conference for the improvement of educational opportunities for children with orthopedic defects who receive their schooling in hospitals and convalescent centers. The conference is being held at the Hotel Ambassador, Atlantic City, N. J., February 26 and 27 in conjunction with the annual convention of the American Association of School Administrators. Teachers in the two hundred and fifty-seven treatment centers of the country that have academic facilities, physicians, school administrators, hospital administrators, staffs of teacher-training centers, nurses, physical and occupational therapists, medical social workers and education program leaders of civic and women's clubs are being invited to attend. Reservations should be made directly with the Hotel Ambassador.

Dr. Ruggles Heads Mental Hygiene Committee.—Dr. Arthur H. Ruggles, Providence, R. I., has been elected president of the National Committee for Mental Hygiene to succeed Eugene Meyer, publisher of the *Washington Post*. Dr. Ruggles resigned January 1 from the superintendency of Butler Hospital, a position that he held for twenty-six years. The board of trustees retained Dr. Ruggles as general consultant. A graduate of Harvard Medical School, Boston, 1906, Dr. Ruggles was appointed assistant superintendent at the hospital in 1909 and superintendent in 1922. He is a consultant in mental hygiene in the department of university health, lecturer in psychiatry at Yale University, New Haven, Conn., and a consultant, U. S. Public Health Service. He is a former president of the American Psychiatric Association, the New England Society for Psychiatry and the Rhode Island Medical Society.

British Journals Available in the United States.—The British Medical Society has appointed Grune & Stratton, Inc., medical publishers, 381 Fourth Avenue, New York 16, as sole agents for the United States of all its periodical publications, beginning January 1948. The journals are the *British Medical Journal*, published weekly, at $14 a year; *Abstracts of World Medicine*, published monthly, $13 a year; the *Abstracts of World Surgery, Obstetrics and Gynecology*, published monthly, $9 a year, and the following quarterlies at $5.50 a year: *Annals of the Rheumatic Diseases; Archives of Disease in Childhood; British Heart Journal; British Journal of Industrial Medicine; British Journal of Pharmacology and Chemotherapy; British Journal of Social Medicine; British Journal of Venereal Diseases; Journal of Clinical Pathology; Journal of Neurology, Neurosurgery and Psychiatry*, and *Thorax*.

Dr. Ida Bengtson Receives Typhus Commission Award.—Ida A. Bengtson, Ph.D., formerly of Bethesda, Md., has been awarded the United States of America Typhus Commission Medal for exceptionally meritorious service during 1943 to 1945 in the investigation and control of rickettsial infections. The award to Dr. Bengtson was made shortly before the recent disbandment of the wartime commission, but presentation was postponed until her return from an extended visit in the West. While associated with the commission, Dr. Bengtson "contributed to the improvement of typhus vaccine, the development of the complement fixation tests and the differentiation of organisms causing various types of typhus fevers." In the ten years before her retirement from the National Institute of Health in January 1946, Dr. Bengtson devoted her investigations to the rickettsial group of diseases and was among the first to study the cultivation of rickettsias in eggs. She was with the U. S. Public Health Service for twenty-six years.

Fellowships Available in Public Health.—Fellowships leading to a master's degree in public health in the field of health education are again being offered to any qualified citizen of the United States between the ages of 22 and 40. Funds are available through a grant from the National Foundation for Infantile Paralysis. Candidates must hold a bachelor's degree and must be able to meet the entrance requirements of the accredited school of public health of their choice. In addition to the bachelor's degree courses in the biologic sciences, sociology and education are required. Training in public speaking, journalism and psychology and work in public health or a related field is considered desirable. The fellowship consists of eight or nine months' academic work, which begins with the fall term in 1948, and three months of supervised field experience in community health education activities in a local health department. Veterans are encouraged to apply and will be paid the difference between their subsistence allowance under the GI Bill of Rights and the monthly stipend of $100 for single veterans or $150 for married veterans. Employees of state or local health departments are not eligible, since federal grants-in-aid are provided through the states for such training. Information may be obtained from the National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

LATIN AMERICA

Two New Medical Journals.—*Journada Medica*, a monthly Argentine medical journal with headquarters at Calle Cordoba 2218, Buenos Aires, recently appeared. Dr. Horacio Basabe is the editor. *Revista Panamericana de Medicina y Cirugia del Torax*, a Spanish quarterly journal with summaries in English, with headquarters at Calle de Amazonas 96, México, D. F., Mexico, recently appeared with Dr. Donato G. Alarcón of that city as editor.

Pan-American Doctors' Club First Scientific Session.—From February 28 to March 1 the Pan-American Doctors' Club will hold its first scientific sessions at the club home, San Miguel Regla, Hidalgo, Mexico. There will be papers on health problems and opportunities for members and guests to enjoy recreational activities. Housing accommodations are limited, but a few nonmember guests can be cared for if reservations are made in advance. For information address Dr. Clarence A. Mills, Secretary, Cincinnati General Hospital, Cincinnati, Ohio.

FOREIGN

International Society of Pathologists.—An international association of societies devoted to clinical pathology was established at meetings in Paris, France, November 21-22 in the course of the first International Congress of the Société Francaise de Biologie Clinique. Delegates and observers attended from Belgium, Czechoslovakia, Denmark, France, Great Britain, Greece, Italy, Peru and the United States. A provisional constitution drawn in general conformance with the rules established by UNESCO for its associated international bodies establishes the governing body of the International Federation as a council or commission of the delegates from the national member societies. The council acts through an Executive Committee of six members. The English and French texts of the statutes will come up for ratification at a meeting of the council, which it is hoped to hold next summer. The conference elected officers as follows: Dr. Sidney C. Dyke, Wolverhampton, England, president; Drs. D. Durupt, France, and Josef Ungar, Czechoslovakia and England, secretaries; Professor Raoul Kourilski, France, vice president, and Dr. W. H. McMenemey, England, treasurer. The second office of vice president was left vacant in the hope that it might be filled by a representative of the United States. The conference defined the term "clinical pathology" as consisting in "the application of pathology and all its related sciences to clinical medicine."

National societies devoted to clinical biology as defined are invited to communicate with the secretary-general, Dr. D. Durupt, 20 Rue de la Pompe, Paris, or the assistant secretary, Dr. J. Ungar, Claxo Laboratories, Greenford, Middlesex, England.

Marriages

JOHN BLACKWELL SUTPHIN, Trenton, N. J., to Miss Caroline Gibbes Hunter in Columbia, S. C., Oct. 17, 1947.

GEORGE CARTWRIGHT ADICKES, York, S. C., to Miss Floride Cantey Des Champs in Columbia, Oct. 18, 1947.

EDWARD G. HASKELL Jr., Jacksonville, Fla., to Miss Gale Deane Shumate of Bluefield, W. Va., recently.

JAMES KEITH PALMER, Sumter, S. C., to Miss Nancy Louise Buie of Rochester, Minn., Sept. 27, 1947.

ANGELA B. ADAMS to Dr. CHESTER R. JABLONOSKI, both of Cleveland, Nov. 12, 1947.

ALLEN WIDOME to Miss Fay Berger, both of Washington, D. C., Feb. 22, 1947.

ROBERT W. TUFFT to Miss Dorothy Galt, both of San Francisco, recently.

Deaths

Max Pinner, Berkeley, Calif.; born in Berlin, Germany, Nov. 28, 1891; Eberhard-Karls-Universität Medizinische Fakultät, Tübingen, Württemberg, Germany, 1920; became instructor in pathology and bacteriology at the University of Illinois College of Medicine in Chicago, later director of laboratories of the Maybury Sanatorium in Northville, Mich., and pathologist at the Herman Kiefer Hospital in Detroit; director of laboratories and research at the Desert Sanatorium in Tucson, Ariz., from 1930 to 1935; diagnostic pathologist for the state tuberculosis hospitals of New York; from 1938 to 1946 on the staff of the Montefiore Hospital for Chronic Diseases in New York; affiliated with Montefiore County Sanatorium in Bedford Hills, N. Y.; served as clinical professor of medicine at Columbia University College of Physicians and Surgeons in New York; specialist certified by the American Board of Pathology; member of the American Sanatorium Association, Society for Experimental Biology and Medicine, American Association for Thoracic Surgery and the American Association for Pathologists and Bacteriologists; fellow of the American College of Physicians; in 1946 awarded the Trudeau Medal of the National Tuberculosis Association; served in the German Army during World War I; author of "Pulmonary Tuberculosis in the Adult"; editor of the *American Review of Tuberculosis*; died January 7, aged 57.

David Robert Climenko, Fort Bayard, N. Mex.; born in New York Aug. 28, 1906; University of Edinburgh Faculty of Medicine, Scotland, 1931; assistant in physiology at the University of Edinburgh from 1929 to 1932; assistant professor of physiology and pharmacology, University of Alberta, Canada, from 1932 to 1934; lecturer in pharmacology at Cornell University in New York, 1934-1935; pharmacologist for the American Cyanamid Company in Stamford, Conn., from 1935 to 1940; pharmacologist for the Winthrop Chemical Company, Rensselaer, N. Y., from 1940 to 1942; associate in biochemistry from 1940 to 1943, later instructor in medicine and research associate in medicine at the Albany Medical College in Albany, N. Y.; served during World War II; affiliated with the Veterans Administration Hospital; died recently, aged 41.

Sidney Isaac Schwab ✠ St. Louis; born in Memphis, Tenn., Nov. 22, 1871; Harvard Medical School, Boston, 1896; later studied at universities in Paris, Berlin and Vienna; professor emeritus of clinical neurology at the Washington University School of Medicine; member and past president of the American Neurological Association; formerly councilor of the medical council of the U. S. Veterans Bureau in Washington; served overseas during World War I; affiliated with St. Louis Children's and Maternity Hospital, Jewish Hospital and the Barnes Hospital; author of "The Adolescent: His Conflicts and Escapes"; on the editorial staff of the *Journal of Nervous and Mental Disease*; died in Boston Nov. 12, 1947, aged 75, of burns.

Earl Cooper, Augusta, Ill.; born in 1879; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1905; member of the American Medical Association; chairman of the county board of assistance; past president of the Hancock County Medical Society; president of the town board of health; physician for the county Selective Service Board during World War II; formerly affiliated with the Illinois Soldiers' and Sailors' Home in Quincy, where he was on the staff of St. Mary's Hospital; served on the staff of the Graham Protestant Hospital in Keokuk, Iowa; died Nov. 5, 1947, aged 68, of coronary thrombosis.

Earl Edward Van Derwerker ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1917; assistant clinical professor of orthopedic surgery at his alma mater; specialist certified by the American Board of Orthopedic Surgery; member of the American Academy of Orthopedic Surgery; fellow of the American College of Surgeons; an officer during World War I; served on the staff of Blythedale Home in Hawthorne, Lawrence Hospital in Bronxville and the Hospital for Special Surgery; died in Newtown, Conn., Nov. 2, 1947, aged 57, of coronary thrombosis.

Louis Storrow Greene ✠ Washington, D. C.; born in 1872; University of Virginia Department of Medicine, Charlottesville, 1895; specialist certified by the American Board of Ophthalmology; served as associate professor of ophthalmology at the Georgetown University School of Medicine; past president of the American Ophthalmological Society; fellow of the American College of Surgeons; head of the eye examining service for the draft board during World War I; affiliated with the Episcopal Eye, Ear and Throat Hospital; died Nov. 12, 1947, aged 74, of coronary thrombosis and cerebral hemorrhage.

Louis Ferdinand Alrutz ✠ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; past president of the Aux Plaines branch of the Chicago Medical Society; served on the staff of West Suburban Hospital in Oak Park; died Nov. 26, 1947, aged 71, of coronary thrombosis.

John Baxter Bain, Lawrence, Mass.; Harvard Medical School, Boston, 1902; member of the American Medical Association; for many years affiliated with Lawrence General Hospital; died in New England Deaconess Hospital, Boston, recently, aged 68, of uremia and myocardial insufficiency.

Harvey M. Beaver, Kansas City, Mo.; Louisville (Ky.) Medical College, 1888; at one time on the faculty of Harvey Medical College in Chicago and the College of Physicians and Surgeons in Kansas City, Kan.; formerly practiced in Huntington, Ind., where he served as county coroner; died recently, aged 87, of interstitial nephritis.

George Crocket Becket, Lakeville, Conn.; Cornell University Medical College, New York, 1900; served on the staff of the Essex County Memorial Hospital in East Orange, N. J.; died in the Hudson City (N. Y.) Hospital Nov. 11, 1947, aged 79, of pulmonary edema and cerebral hemorrhage.

Joseph Jackson Blitch, Yonges Island, S. C.; University of the South Medical Department, Sewanee, Tenn., 1901; died in Charleston recently, aged 79.

Charles Arthur Brake, Norman, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1917; member of the American Psychiatric Association; served during World War I; assistant professor of psychiatry at the University of Oklahoma School of Medicine; affiliated with the Central Oklahoma State Hospital; died recently, aged 52, of cerebral hemorrhage.

James Cooper Bright, Fall River, Mass.; Jefferson Medical College of Philadelphia, 1907; member of the American Medical Association; died in the State Hospital, Taunton, Nov. 12, 1947, aged 74, of arteriosclerotic heart disease.

James Blaine Brown, Pell Lake, Wis.; Loyola University School of Medicine, Chicago, 1916; died Nov. 8, 1947, aged 63, of acute coronary occlusion.

William Turner Carstarphen ✠ Westport, Conn.; Jefferson Medical College of Philadelphia, 1904; member of the Medical Society of the State of New York; at one time on the faculty of Wake Forest (N. C.) College; served during World War I; chief medical officer at the Japanese-American camp in Arkansas and Colorado during World War II; died in the Kingston (Ontario) General Hospital Nov. 2, 1947, aged 72, of carcinoma of the rectum.

Simeon Cohen, Meriden, Conn.; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1921; died in the Meriden Hospital Nov. 2, 1947, aged 52 of malignancy of right testicle.

Ross Alvah Cooper, Carmel, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; member of the American Medical Association; served during World War I; member of the staff of the Methodist Hospital in Indianapolis, where he died Nov. 8, 1947, aged 65, of cerebral hemorrhage.

James Harry Cox, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; died in the Veterans Administration Hospital, Dearborn, Nov. 24, 1947, aged 75, of arteriosclerotic heart disease.

Harry Lee D'Arms, Hector, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1892; served as county coroner; died recently, aged 79, of uremia.

Charles A. Davis, Kennedy, Ala.; Birmingham Medical College, 1912; member of the American Medical Association; died recently, aged 63.

Jules Jehin De Prume, New York; Université de Paris Faculté de Médecine, France, 1893; Laval University Faculty of Medicine, Quebec, Canada, 1894; affiliated with the Misericordia Hospital; died in the French Hospital Nov. 11, 1947, aged 77, of carcinoma of the large intestine.

Robert Cecil Donham, Beverly Hills, Calif.; University of Southern California School of Medicine, Los Angeles, 1933; member of the American Medical Association; served an internship and residency at the Los Angeles County General Hospital in Los Angeles, where he was a member of the surgical staffs of the California Lutheran and the Methodist hospitals; died recently, aged 43.

John Rose Dyson ✠ Hazleton, Pa.; Medico-Chirurgical College of Philadelphia, 1897; served on the staff of the Hazleton State Hospital; died Nov. 18, 1947, aged 73, of coronary thrombosis.

Rebecca Mortimer Evans, Denton, Texas; Northwestern University Woman's Medical School, Chicago, 1902; died Oct. 30, 1947, aged 75, of cerebral hemorrhage.

Victor Finsand ✠ San Francisco; University of Illinois College of Medicine, Chicago, 1916; served during World War I; died Nov. 2, 1947, aged 58, of cerebral hemorrhage.

Solomon Greenspahn, Chicago; Rush Medical College, Chicago, 1889; member of the American Medical Association; medical director and treasurer of the American Hospital; died Nov. 17, 1947, aged 80, of coronary thrombosis.

Frank West Harrah ✠ Columbus, Ohio; Cornell University Medical College, New York, 1920; member of the American Urological Association and the Columbus Academy of Medicine; fellow of the American College of Surgeons; affiliated with Grant, White Cross and Mount Carmel hospitals; died Nov. 6, 1947, aged 55, of cerebral hemorrhage.

Joseph A. Heintzelman, Philadelphia; Georgetown University School of Medicine, Washington, D. C., 1902; died in the Lankenau Hospital Nov. 7, 1947, aged 69, of subacute bacterial endocarditis and bronchopneumonia.

Howard Crosby Hoff, New York; Columbia University College of Physicians and Surgeons, New York, 1907; served on the staffs of West Park and St. Elizabeth's hospitals; died Nov. 21, 1947, aged 63, of coronary thrombosis.

Tarlton Ambrose Hood, Garnett, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1897; member of the American Medical Association; served overseas during World War I; served as county health officer, member of the board of education and chamber of commerce; died Nov. 3, 1947, aged 75, of undulant fever.

William W. Hume, Beckley, W. Va.; University of Virginia Department of Medicine, Charlottesville, 1901; member of the American Medical Association; served as vice president of the West Virginia Public Health Association; for many years county health officer; died Nov. 4, 1947, aged 81, of pneumonia.

J. Newton Hunsberger ✠ Norristown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1889; member of the House of Delegates of the American Medical Association from 1923 to 1943; served as chairman of the board of trustees of the Montgomery County Medical Society; past president of the Valley Forge Historical Society; affiliated with the Montgomery Hospital; died Nov. 1, 1947, aged 80, of cerebral hemorrhage.

Ernest Hart Judd ✠ Springfield, Mass.; Tufts College Medical School, Boston, 1912; medical consultant at the Springfield Hospital; died recently, aged 62, of coronary occlusion.

Dillon James Kennington ✠ Michigan City, Ind.; Indiana University School of Medicine, Indianapolis, 1937; assistant physician at the Indiana State Prison Hospital; on the staff of St. Anthony's Hospital, where he died Nov. 2, 1947, aged 35, of heart disease.

Edmund Carl Konrad, Cleveland; University of Wooster Medical Department, Cleveland, 1908; served during World War I; affiliated with the Lutheran, Evangelical Deaconess, Grace and Charity hospitals; died recently, aged 63, of coronary thrombosis.

Martin Kutscher ✠ New York; born in Stapleton, N. Y., Aug. 22, 1883; Columbia University College of Physicians and Surgeons New York, 1905; clinical professor of medicine and associate attending physician at the New York Polyclinic Medical School and Hospital; member of the American Heart Association and the Association for the Study of Internal Secretions; served on the staffs of the City, Lebanon and Midtown hospitals; died recently, aged 64, of myocardial infarction.

Alfons Frederick Landeker ✠ New York; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1911; died recently, aged 61, of myocarditis.

Edwin F. Landy, Cincinnati; Medical College of Ohio, Cincinnati, 1891; formerly on the faculty of his alma mater; veteran of the Spanish-American War; died Nov. 21, 1947, aged 79, of cerebral arteriosclerosis.

William James Larkin, Chicago; Rush Medical College, Chicago, 1922; member of the American Medical Association; affiliated with St. Francis Hospital in Evanston, Ill.; died in Galesburg, Ill., Nov. 24, 1947, aged 65, of coronary sclerosis.

Lyder Laurits Laugeson, San Diego, Calif.; University of Minnesota Medical School, Minneapolis, 1929; member of the American Medical Association; served during World War II; died Nov. 11, 1947, aged 44, of nephrosis and cirrhosis of the liver.

E. Oscar Lindenmuth ✠ Indianapolis; Medico-Chirurgical College of Philadelphia, 1906; died in Methodist Hospital recently, aged 75, of uremia and prostatic hypertrophy.

Charles Oscar Lindstrom ✠ Eagle River, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; graduate in pharmacy; formerly vice president and on the staff of Columbus Hospital in Chicago; health officer; died Nov. 3, 1947, aged 72, of heart disease and pneumonia.

James A. Long, Oxford, Ohio; University of Louisville (Ky.) Medical Department, 1892; member of the American Medical Association and the Indiana State Medical Association; for many years secretary of the board of health in Anderson, Ind.; died in Mercy Hospital, Hamilton, Ohio, Nov. 9, 1947, aged 87, of cardiovascular renal disease.

Leo Martin Maguire, Minneapolis; John A. Creighton Medical College, Omaha, 1912; lieutenant colonel, medical corps, Army of the United States, affiliated with the Veterans Administration during World War II; at the time of his death medical officer for Veterans Administration; died Nov. 10, 1947, aged 59, of injuries received when he fell through a trap door at a hunting club near Minneapolis.

Reuben Maurits ✠ Grand Rapids, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; member of the American Society of Anesthetists; past president of the Grand Rapids Society of Anesthesiology, which he helped organize; served on the staffs of Butterworth Hospital and Blodgett Memorial Hospital, where he died Nov. 11, 1947, aged 77, of subarachnoid hemorrhage and arteriolar nephrosclerosis.

William Dennis McClung, Huntington, W. Va.; College of Physicians and Surgeons, Baltimore, 1907; served in the U. S. Public Health Service during World War I; formerly superintendent of the Spencer (W. Va.) State Hospital and the Huntington State Hospital; died Nov. 2, 1947, aged 71, of injuries received in a fall from a moving automobile at Dickson.

Charles Hugo McKenna, Chicago; Northwestern University Medical School, Chicago, 1913; member of the American Medical Association; fellow of the American College of Surgeons; affiliated with Holy Cross Hospital; died recently, aged 60, of bronchogenic carcinoma of the lung.

Nejll Henry McLeod Jr., Raleigh, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1930; member of the American Medical Association; served during World War II; died recently, aged 42, of heart disease.

Clarence Sherman Massey, Wadesboro, N. C.; Howard University College of Medicine, Washington, D. C., 1925; died recently, aged 48, of pneumonia.

James Graham Maxwell, Reno, Nev.; Colorado School of Medicine, Boulder, 1897; died in a hospital at Colorado Springs, Colo., recently, aged 78, of pneumonia.

Diedrich Janssen Meents ✠ Fort Madison, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; took postgraduate work at Harvard, Berlin and Vienna; at one time assistant professor of pathology and bacteriology at the State University of Iowa; died Nov. 6, 1947, aged 69, of coronary occlusion.

Arthur Nourse Meloy, Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1905; died in the Providence Hospital Nov. 1, 1947, aged 75, of subdural hematoma.

George Washington Michell ✠ Peoria, Ill.; Rush Medical College, Chicago, 1902; medical director of the Michell Farm and the Michell Sanatorium; died Nov. 17, 1947, aged 71, of cerebral hemorrhage.

Philip Earl Moody, Detroit; Detroit College of Medicine, 1902; served on the staffs of the Harper, Crittenden and Providence hospitals; died Nov. 11, 1947, aged 68, of coronary thrombosis.

Hugh Montgomery Orr, La Salle, Ill.; College of Physicians and Surgeons, Baltimore, 1895; for many years mayor; a founder of St. Mary Hospital; died Nov. 16, 1947, aged 80, of heart disease.

Albert L. Nason, Darling, Miss.; Chattanooga (Tenn.) Medical College, 1905; died in the Baptist Memorial Hospital, Memphis, Tenn., recently, aged 77, of cerebral thrombosis.

Clara Mary Ochs, Oak Park, Ill.; University of Illinois College of Medicine, Chicago, 1918; member of the American Medical Association; served on the courtesy staff of the Woman and Children's Hospital in Chicago; died Nov. 19, 1947, aged 71, of carcinoma of the cecum.

David Wilmot Overton, Avon Park, Fla.; University and Bellevue Hospital Medical College, New York, 1899; died recently, aged 80.

Jennie Leigh Kellogg Paris, Hammondsport, N. Y.; University of Buffalo School of Medicine, 1893; died recently, aged 79, of embolism following fracture of femur.

Albert Taylor Parrish, Ovid, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1881; served as health officer; died recently, aged 89, of senility.

John Patterson, Lexington, Ky.; Hospital College of Medicine, Louisville, 1900; died recently, aged 69, of heart disease and Parkinson's disease.

Merton S. Pearre, St. Petersburg, Fla.; University of Maryland School of Medicine, Baltimore, 1900; died in the Suburban Hospital, Bethesda, Md., Nov. 1, 1947, aged 75, of cerebral hemorrhage.

Benjamin Lane Phillips, Paola, Kan.; University of Kansas School of Medicine, Kansas City, 1907; served as county coroner; died recently, aged 66, of congestive heart failure.

William Giles Phipps, Mount Vernon, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1913; served during World War I; affiliated with Mount Vernon Hospital; died Nov. 2, 1947, aged 61, of myocarditis.

William Aloysius Pindar, North Bergen, N. J.; University and Bellevue Hospital Medical College, New York, 1909; for many years police surgeon; served as a member of the state board of medical examiners and city board of health; medical examiner for selective service during World War II; affiliated with St. Mary's Hospital in Hoboken; died Nov. 12, 1947, aged 63, of coronary thrombosis.

Minor Gibson Porter ✠ Baltimore; University of Maryland School of Medicine, Baltimore, 1886; past president of the Baltimore County Medical Society; medical officer of the county draft board during World War I; formerly mayor of Lonaconing; affiliated with the Church Home and Infirmary and Union Memorial Hospital, where he died recently, aged 82, of a fractured right hip as the result of a fall, bronchopneumonia, and diabetes mellitus.

Randolph Raynolds ✠ Wallingford, Conn.; Columbia University College of Physicians and Surgeons, New York, 1914; served during World War I; formerly affiliated with the Meriden State Tuberculosis Sanatorium in Meriden and the Veterans Home Hospital in Rocky Hill; died recently, aged 61, of coronary occlusion.

Donald Ford Robertson, Rahway, N. J.; Washington University School of Medicine, St. Louis, 1929; associate medical director of Merck & Co., Inc.; died in the Harkness Pavilion, Presbyterian Medical Center, New York, Nov. 8, 1947, aged 44, of leukemia.

Charles Edward Rooney ✠ Santa Monica, Calif.; Creighton University School of Medicine, Omaha, 1905; formerly on the faculty of his alma mater; served on the staffs of Santa Monica and St. John's hospitals; at one time practiced in Yuma, Ariz., where he was physician for the Southern Pacific Company and county health officer; died Nov. 1, 1947, aged 66, of hypertensive heart disease.

William Walter Sames, Hartshorne, Okla.; Missouri Medical College, St. Louis, 1896; member of the American Medical Association; formerly affiliated with the Indian Service; died recently, aged 84.

Paul Henry Sandresky ✠ Buffalo; University of Buffalo School of Medicine, 1911; formerly a minister; affiliated with the Lafayette General Hospital and the Millard Fillmore Hospital, where he died Nov. 16, 1947, aged 68, of acute myocardial infarction.

Thomas H. Sandy, Chicago; Harvey Medical College, Chicago, 1901; member of the American Medical Association; physician for the Continental Illinois National Bank and Trust Company for many years; died at his home in Forest Park, Ill., Nov. 24, 1947, aged 72, of coronary occlusion and arteriosclerosis.

Frederick J. Schaufelberger, Los Angeles; Jefferson Medical College of Philadelphia, 1884; died Nov. 20, 1947, aged 97.

Ernest Edward Schriefer, Cannelton, Ind.; University of Louisville (Ky.) Medical Department, 1906; member of the American Medical Association; past president of the Perry County Medical Society; formerly health officer; medical examiner for the county draft board during World War I; affiliated with the Parkview Hospital, Tell City, where he died, Nov. 3, 1947, aged 67, of cerebral hemorrhage.

Erich Wilhelm Schwartze, Washington, D. C.; Rush Medical College, Chicago, 1914; member of the American Medical Association and the Medical and Chirurgical Faculty of Maryland; at one time professor of physiology and pharmacology at the University of Georgia School of Medicine in Augusta and the University and Bellevue Hospital Medical College in New York; died in the Providence Hospital Nov. 11, 1947, aged 56, of coronary thrombosis.

James Wilbur Shankland, St. Louis; St. Louis University School of Medicine, 1904; served during World War I; formerly city hospital commissioner; at one time on the staffs of the Missouri Baptist and St. John s hospitals; died Nov. 7, 1947, aged 80, of heart disease.

Ernst Simmel, Los Angeles; Universität Rostock Medizinische Fakultät, Rostock, Mecklenburg, Germany, 1908; member of the American Psychoanalytic Association; honorary president of the Los Angeles Psychoanalytic Society; died Nov. 11, 1947, aged 65, of heart disease.

Minabel Snow, Brecksville, Ohio; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1899; died recently, aged 82, of pneumonia.

John Howard Snyder, Sunbury, Pa.; Illinois Medical College, Chicago, 1902; medical examiner for the Pennsylvania Railroad; died in Sacred Heart Hospital, Allentown, recently, aged 73, of myocardial infarction.

Dallas Southard ✠ Stamford, Texas; University of Tennessee College of Medicine, Memphis, 1911; served in France during World War I; affiliated with Stamford Sanitarium; died in Pleasant Hill recently, aged 65, of coronary thrombosis.

Erwin Straehley ✠ Cincinnati; Medical College of Ohio, Cincinnati, 1889; affiliated with the Christ and Deaconess hospitals; at one time assistant health officer; for many years member of the board of trustees of the University of Cincinnati; died in Good Samaritan Hospital Nov. 6, 1947, aged 79, of carcinoma of the rectosigmoid.

Joseph Toal ✠ Ridgefield, N. J.; Syracuse University College of Medicine, 1927; affiliated with the Englewood Hospital, where he died recently, aged 56, of coronary thrombosis.

Ansel Harry Tulupan, Chicago; Loyola University School of Medicine, Chicago, 1925; died Nov. 27, 1947, aged 47, of coronary thrombosis.

Arthur Henry Weis, Chicago; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1901; served during World War II; on the staff of the Columbus Memorial Hospital; health editor of the *Abendpost*; died in Mount Sinai Hospital Nov. 10, 1947, aged 74, of virus pneumonia.

William Whitridge Williams ✠ Denver; Johns Hopkins University School of Medicine, Baltimore, 1899; specialist certified by the American Board of Pathology; served as a member of the state board of medical examiners, of which he had been secretary-treasurer; affiliated with the Denver General, City and County and St. Luke's hospitals; died recently, aged 71.

Preston Ezekiel Wolfe, Abingdon, Va.; University of the City of New York Medical Department, New York, 1890; died recently, aged 84, of cerebral anemia and arteriosclerosis.

Robert Henry Wymer ✠ Altoona, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1921; during World War I served in the student army training corps; an examining physician for the Selective Service System during World War II; member of the staff of the Mercy Hospital; died recently, aged 49, of coronary thrombosis.

DIED WHILE IN MILITARY SERVICE

John Charles Gaffney Jr. ✠ Assistant Surgeon, Lieutenant (jg) U. S. Navy, Du Bois, Pa.; Loyola University School of Medicine, Chicago, 1943; began active duty in the U. S. Navy in May 1943, interning at the Naval Hospital in Key West, Fla.; died in a typhoon in the Asiatic area Dec. 18, 1944, aged 28.

John Richard Siddall, Riverton, N. J.; Jefferson Medical College of Philadelphia, 1937; member of the American Medical Association; interned at the Cooper Hospital in Camden; served a residency at the Sloane Hospital for Women in New York; began active duty as a first lieutenant in the medical corps, Army of the United States, in May 1942; promoted to captain; died on Ascension Island May 10, 1945, aged 34, of asphyxia and third degree burns received in a plane crash.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 27, 1947.

Prevention of Meningitis Following Spinal Puncture

The Public Health Laboratory Service and the London Sector Pathologists' Committee has issued a memorandum on the avoidance of the meningitis which results from inoculation into the spinal canal of microbes in the operation of withdrawal of cerebrospinal fluid or in the induction of spinal anesthesia. The organisms most frequently incriminated are Pseudomonas aeruginosa and related organisms which can multiply in water at room temperature. Less frequently staphylococci and other skin contaminants are responsible. The sources of contamination are (1) apparatus insufficiently sterilized or contaminated during use; (2) so-called sterile water or saline solution used to rinse the apparatus; (3) hands of the operator or his assistants; (4) skin of the patient, and (5) anesthetic, antibiotic or other solutions.

For prevention the ideal would be to adopt the full antiseptic ritual of a surgical operation. But in many cases time and place render this impossible. The following measures are therefore recommended as practical in nearly all circumstances. If facilities are available, all apparatus, including manometer, should be enclosed within suitable containers and sterilized either by autoclaving at 15 to 20 pounds (6.8 to 9.1 Kg.) pressure for twenty minutes or by dry heat at 160 C. for an hour. The complete outfit can then be held ready for use at any time. If dry heat is used the rubber tubing of the manometer should be sterilized by boiling. For syringes and needles dry heat is preferable but ordinarily necessitates all-glass syringes. If autoclaving or sterilization by dry heat cannot be employed, all apparatus should be sterilized immediately before the operation by boiling for five minutes, preferably in distilled water. A sterilizer with a perforated lift-up tray should be used. At the end of the boiling the tray is removed, placed in the inverted lid, covered with a sterile towel and left to cool. In emergencies a perfectly clean saucepan with a lid can be used. After boiling the water should be drained off and the saucepan left with the lid on until cool. Chemical disinfection, such as soaking in alcohol, should not be used.

The operator should scrub up as for a major operation, or should don dry sterile gloves. If gloves are not available his hands should be dry before he handles any apparatus. This may be accomplished by rinsing with industrial alcohol and/or drying with a sterile towel. Where needle and syringe have to be assembled, the needle should be handled with sterile forceps. From this point onward the operator should touch nothing except the sterile instruments and the skin of the patient. The trochar when withdrawn should be laid on a sterile towel; otherwise it may infect the spinal fluid if introduced again to clear the needle. The skin of the patient should be thoroughly washed with soap and warm water, followed by thorough swabbing with tincture of iodine or 70 to 90 per cent alcohol.

Sir Bernard Spilsbury

Sir Bernard Spilsbury, who for thirty years was the foremost medicolegal pathologist and was employed by the police to investigate the cause of death in all the notorious crimes, was found dying in his laboratory at University College, London. The room was filled with illuminating gas. He had reached the age of 70 and had been in ill health for some time. The coroner's verdict was that he had turned on the gas while his mind was deranged. He retired from his position as government pathologist in 1934 but had continued to work as honorary pathologist and to lecture. His position was unique. Between the two wars there was hardly a case in which the painstaking collection of evidence was required for the conviction of a murderer in which he was not employed. A striking example was the sensational "Brides in the Bath" case. A man and his newly wedded wife were living in lodgings. In the morning while she was taking a bath he went out, according to his own account, to buy fish. On his return he raised an alarm in the house because, according to his account, he had found his wife collapsed in the bath. She was drowned, and at the inquest his version was accepted and it was supposed that the woman had fainted in the tub and then was drowned. But when a second wife and later a third wife died in the same way, suspicion was aroused and Spilsbury was called in by the police. He came to the conclusion that the women had been murdered by the husband's seizing their feet and suddenly raising them, which would drag their heads under the water. They would be drowned without being able to cry out and alarm the other occupants of the house. To test his hypothesis Spilsbury experimented with a nurse, who, clad in bathing suit, entered a bath full of water. Spilsbury suddenly lifted her feet. She nearly died and had to be revived by artificial respiration. The husband was convicted of murder. No such method of murder was ever known before or since this crime.

Another notorious case was that of "Dr." Crippen. His wife had disappeared, and human remains which could not be identified were found in the cellar of Crippen's house in London. A fraction of a grain of scopolamine hydrobromide was isolated from the remains, and he was convicted of murder.

PALESTINE

(From Our Regular Correspondent)

JERUSALEM, Dec. 15, 1947.

The Rh Factor Among Jewish Communities

In a study on the Rh factor, Gurevitch, Sadowsky, Brzezinzky and Polishuk of the Rothschild Hadassah University Hospital found great variations in the incidence of the Rh factor among the different Jewish communities in Jerusalem. Among 1,913 women examined, only 9.6 per cent were Rh negative. Among 12,645 deliveries during a period of eight years only 6 cases of erythroblastosis fetalis were observed. On the basis of these figures the rate of erythroblastosis fetalis among Rh-negative women was 1 : 210, which compares with a rate of 1 : 25 to 1 : 50 reported elsewhere. Of special interest may be the low rate of Rh-negative women found in the Yemenite and Kurdish-Persian communities. Of 44 Yemenite women examined, only 1 was found to be Rh negative, i. e., 2.3 per cent; an even lower rate of 1.5 per cent Rh-negative persons was found among 203 Kurdish-Persian women. These two groups are characterized by their segregated mode of life, intermarriage is rare among them. It is significant that not a single case of erythroblastosis fetalis has been observed among 310 deliveries in Yemenite Jewesses and 1,739 deliveries among Kurdish-Persian Jewesses in the obstetric department of this hospital during the last six years.

In a study of the Rh factor among women suffering from habitual abortion, toxemia of pregnancy, stillbirths and prematurity, the rate of Rh-negative women was similar to that observed in the population at random. In a group of 22 women with obstetric histories suggestive of Rh incompatibility only 3 Rh-negative patients have been found. No case of erythroblastosis fetalis and no signs of isoimmunization in the mothers have been observed in this group.

A detailed study was made in a group of 32 Rh-negative multiparas with obstetric histories of six to fourteen pregnancies. The total of pregnancies in this group was two hundred and seventy-nine. All the husbands except three were homozygous. No case of erythroblastosis fetalis and no signs of isoimmunization in the mothers have occurred in this group.

Allergic Warm Season Conjunctivitis

Conjunctivitis vernalis was the designation given to conjunctivitis appearing periodically in Palestine and reported every year. During the Congress of the Jewish Medical Association in 1944 M. J. Gutmann reported on this disease (*Acta med. orient.* **4**:150 [May] 1945), calling it an allergic warm season conjunctivitis, as it appears during the months from February to November, in other words during the warm season, and practically disappears with the beginning of rain. The cause of this conjunctivitis is allergic; usually there is a chronic infection with a secondary fungous allergy. The most common fungi are of the following families: Alternaria, Hormodendrum, Cladosporium, Penicillium, Aspergillus and Monilia. The disease usually attacks young persons. Girls are apparently less susceptible than boys. Forty-five per cent of all patients were from 5 to 15 years of age.

The treatment primarily is aimed at removing the focus of infection and desensitizing the patients with a mixed extract of various molds and bacteria. Within six months—sometimes only after one to two years—two thirds of the patients could be freed of their symptoms. The therapy, however, is not entirely reliable. Gutmann stated that there are still many unsolved problems in connection with allergic warm season conjunctivitis.

In a paper just published (*Acta med. orient.* **6**:167 [May] 1947) Gutmann points out that riboflavin given in 5 mg. injections daily proved particularly effective in influencing the inflammation and itching of the eyes. He compares the effect of riboflavin with that of epinephrine in an attack of asthma. The desired effect was reached ten to thirty minutes after the injection of riboflavin and could be maintained for twelve to fourteen hours. The administration of riboflavin in tablet form did not produce relief, but fresh yeast often proved to be successful. Symptoms of riboflavin deficiency could not be found.

TURKEY

(From Our Regular Correspondent)

ANKARA, Dec. 22, 1947.

Aid to Egypt During the Recent Cholera Epidemic

The sudden outbreak of cholera in Egypt during the last week of September 1947 placed Turkey in a difficult position. For the first time in eight years Turkish pilgrims were on their way to Mecca, and many others were in the midst of preparations to procure their passports. Moreover, the eve before "Kurban Bairam" was on a Friday, which naturally made the pilgrimage all the more desirous. Almost 8,000 Mohammedans from Turkey alone had decided to make the pilgrimage this year.

Turkey had not had any cholera for years, and all the anticholera vaccine on hand had been sent during the war to China, where it was urgently needed. At the Refik Saydam Institute (Central Institute of Hygiene) the preparation of anticholera vaccine was at once undertaken. The pilgrims and the inhabitants along the coast and at the southern borderline of Syria were vaccinated, and during the first week of October a physician, two trained nurses and four sanitary inspectors, equipped with vaccine for 500,000 persons, left Ankara for Egypt by air. Vaccine sufficient for 200,000 persons was forwarded soon afterward to Syria. The expedition is still working in Egypt in localities indicated by the Egyptian government.

Obviously, with cholera in Egypt, the scourge might easily find its way into Turkey. The Ministry of Health at once organized a cholera prevention board with representatives from the Ministry of National Defense, the Ministry of Communication and the Ministry of the Interior meeting every other day to get first hand information concerning the epidemic in Egypt and the state of health of the Turkish pilgrims. As a precautionary measure the work at the Central Institute of Hygiene proceeded on a twenty-four hour schedule to produce a sufficient quantity of immediately available vaccine. Vaccination teams were organized to work all through the night, and all personnel on land, sea and air transportation systems, the whole population of the coastline provinces and all tradespeople handling food were immediately vaccinated. Measures were taken to insure the return of the pilgrims by a route other than Egypt and likewise that those returning by air alight only at the Istanbul landing field. Passenger boats were sent from Istanbul and Smyrna to the ports of Cidda Jidda and Beirut with the strictest order to take on no other passengers than Turkish pilgrims arriving there by land. At the Smyrna and Istanbul ports the returning pilgrims were quarantined, vaccinated and searched for carriers. All food that the pilgrims brought with them, even the water from the holy well in Mecca and the dates, was destroyed and special emphasis was given to disinfection of means of transportation, clothing and other possessions of the pilgrims and to the destruction of noxious insects or vermin with DDT. Through articles in the daily papers and radio talks the public was enlightened as to the nature of cholera; films were shown, posters and leaflets were distributed.

Great vigilance was necessary, and drastic measures had to be taken by the Nusaybin and Islahiye health authorities to prevent the scourge from coming in by these southern Syrian gates, for it was reported that pilgrims attempted to cross the border clandestinely in railway trains, automobiles, omnibuses, wagons, on horseback and on foot.

To insure a plentiful supply of anticholera vaccine the Ministry of Health set aside two more laboratories for its production, one in Istanbul and one in Smyrna. This made it possible to meet the Turkish needs and come to the assistance of Egypt, Syria and other countries.

Through the interest people are now taking in regard to matters of health as a result of education and health propaganda, and through the health organization of the Turkish republic, it has been possible to avert this terrible scourge and assist neighboring countries as advocated in the constitution of the World Health Organization of the United Nations.

"Paludrine" and "Quipenyl" Therapy in Malaria

Results concerning the treatment of malaria with the new remedies "paludrine hydrochloride" (chlorguanide hydrochloride) and "quipenyl" at the Ministry of Health's Adana Malaria Institute have been published by Dr. Celal Gokberk, chief of the institute's laboratory. Neither single dose nor daily continual doses of 0.75 or 1 Gm. of "paludrine" for adults have produced toxic effects. Children above 8 years of age were given 0.1 Gm. twice daily; the same dose was also given to a delicate child aged 3 years and to a child aged 12 years with no untoward results. The blood chemical formula in 11 patients revealed no abnormal conditions; after treatment a 9 per cent reticulocytic crisis was found in 1 patient, 7 per cent in another. Urinanalysis was normal on admission and on discharge. In 10 ambulant cases of benign tertian malaria (due to Plasmodium vivax) a single dose of two to three tablets was given and patients recovered within a month, but after a short interval there were some recurrences and a single tablet then had no effect. In the malignant form of tertian malaria (due to Plasmodium falciparum) "paludrine" was not satisfactory; parasites in the blood diminished greatly and a second attack was forestalled, but in from seven to ten days there were recurrences. At the institute hospital in 11 of 12 cases of benign malaria the remedy was effective in preventing a second attack; in the 1 case in which the results were unsatisfactory, a great many parasites were present in the blood. In the morning and evening blood examination of 8 patients the parasites had completely disappeared within three days, in 5 patients within two days. Splenic punctures were performed in 2 cases, revealing the presence of parasites on the fourth day in 1 case, while the other was negative. In 1 case of vivax and falciparum (mixed) malaria there was a second attack which came to a halt on the third day. In 9 of

13 cases of tertian malaria due to P. falciparum second attacks occurred. In 2 of the other 4 cases the parasites in the circulating blood had disappeared on the second day, in 3 on the seventh and in 4 on the fourth day. How far the new remedy is effective evidently depends on the concentration of parasites in the blood. In 1 of 3 patients on whom a splenic puncture was performed the parasites disappeared on the sixth day and in the other 2 on the fourth day. In 2 cases in which a bone marrow puncture was performed, the parasites had disappeared on the fourth day. For examination of the blood the drop and the smear methods were employed, using the original Giemsa solution for staining. During a second attack of malaria tropica the chromatin rings had taken the dye only slightly, and the widening and disappearance of the chromatin granules was observed. The protoplasm had also taken the dye only slightly, and patches devoid of chromatin were visible. The formation of new rings from degenerated adult parasites in benign tertian malaria has not been observed. Blood examination of patients under treatment were made twice and three times during twenty-four hours, and during from three to seven days. In malaria tropica "paludrine" had no effect on schizonts or gametes.

"Quipenyl," a malaria remedy on a "plasmochin" (pamaquine naphthoate) basis, was also given a trial in 2 cases due to P. vivax, 2 cases due to P. falciparum and 1 case due to mixed tertiana-tropica infection. Three times daily these patients were given a 0.01 Gm. tablet of the drug, resulting in the disappearance of the gametes. Though in the chronic cases the gametes disappeared in the blood stream it was not possible to prevent the formation of new gametes, which were again made to disappear with "quipenyl." In 3 of the 5 cases, gametes disappeared on the third day; in 1 chronic case they disappeared on the fourth day but reappeared on the fifth. This patient was again given "quipenyl," and on the eighth day the blood was completely free from gametes. It was observed that the protoplasm and chromatin granules had taken the dye only slightly and that the remedy had no effect on pigmentation.

BUENOS AIRES

(From Our Regular Correspondent)

Jan. 10, 1948.

The Galli-Mainini Pregnancy Test

At the Congress of Obstetrics and Gynecology of the Rio de la Plata, in Buenos Aires, Dr. Carlos Galli-Mainini communicated further important data on his new test for pregnancy (THE JOURNAL, Oct. 11, 1947, p. 374). The basis of the test is the phenomenon of liberation and migration of spermatozoa of the toad, a direct effect of the administration of gonadotropin. The subcutaneous injection of 10 cc. of urine of a pregnant woman into the lymphatic sac provokes, due to its content of chorionic gonadotropin, the liberation of spermatozoa which in the adult toad normally are fixed at the Sertoli cells. The already free spermatozoa pass through the vas deferens and certain renal glomeruli and appear in the urine, where they are then found as described in THE JOURNAL, Aug. 2, 1947, page 1196.

The male toad is smaller than the female, its color is darker and more uniform, its skin more rugged, its forearm thicker; it croaks when taken by the sides; it has a dark brown pigmentation on the inner side of the thumb and has the embrace reflex. It is easy to handle and to keep, without alimentation, in a pool for months; it only needs a humid surrounding.

Factors which are important for the reaction include the weight of the toad, which should not be under 100 Gm. The minimum dose is apparently about 40 units of chorionic gonadotropin; a greater quantity is necessary if serum gonadotropin is used. The division into fractions of a dose which is insufficient when given all at once does not increase the capacity of the reaction. Low temperatures delay the reaction, while darkness apparently is favorable.

The test is positive with chorionic and serum gonadotropin, with hypophysis of the toad, the rat and the rabbit, and also with the bovine follicle-stimulating hormone. It is negative with the urine of normal men and women, children and aged persons; with gynecologic or endocrine disorders; with estrogens, progesterone, testosterone, thyroxin, desoxicorticosterone, beta-hypophamine ("pitressin"), epinephrine, adrenocorticotropin, corticotropin, prolactin; hypophysis of cattle, dog and pig, of Crotalus terrificus; with serum and urine of pregnant sheep, cow, mare or hog; with suspension of tissue of liver, kidney, adrenal gland, spleen, heart, gastrointestinal tract, muscles, intermediate lobe of hypophysis; with zinc sulfate, methylene blue, acetylcholine and copper acetate.

The results obtained from 1,354 tests in the first four months of pregnancy were 99.56 per cent correct with not one false positive result. The toxicity of the female urine for the toad is very low (0.95 per cent mortality). Among 281 tests made simultaneously with the Friedman test, 19 results did not coincide. In 2 of them it could not be established if the toad or the rabbit proved correct; in 2 others the rabbit was correct, and in 15 others, the toad. Among 123 women pregnant from six to nine months the percentage of positive results was less. The positivity was better with urine than with serum.

In quantitative investigations it was found that the test was still positive in some cases with as little as 0.125 cc. of urine, while in other cases as much as 4 cc. was necessary. Other quantitative studies showed that the urine lost little of its gonadotropic potency at normal temperature until after ten days.

Of 385 positive tests, 88 per cent could be determined within two hours.

With respect to urine, the test is only positive with urine of pregnant women or with mole (2 cases) or chorionepithelioma (2 cases).

The result is always clearly positive or negative, through the presence or absence of spermatozoa. The technic is simple, without previous preparation of patient or urine. Special microscopic technic is not necessary, and differentiation of the spermatozoa is easy. The test animals are inexpensive, do not need special attention and can be used repeatedly.

In the discussion the eleven communications on this subject confirmed the statements of Dr. Galli-Mainini. They referred to experiences with 150 to 470 tests carried on by each author.

Orthopedic Traction on the Skeleton

Dr. Carlos E. Ottolenghi, associate professor of orthopedic surgery, Faculty of Medicine of Buenos Aires, has completed an investigation for which he has just received the prize which is annually awarded by the Argentine Society of Surgeons. Ottolenghi studied in dogs and rabbits, as well as clinically, the tolerance of the organism for iron wire and traction, particularly the reactions of the tissues, the histopathologic changes, the technic of application and the resistance of different kinds which the wire has to overcome, the direction of the traction powers and the application of wire in children. Infection and exaggerated traction are the most important dangers of traction on the skeleton. He prefers to put the wires in tension according to Kirschner's technic without using the nails of Steinmann.

Brief Items

The first Argentine Congress of Bronchoesophagology was held under the honorary chairmanship of Professor Chevalier L. Jackson of Philadelphia, who gave courses in Buenos Aires and in Córdoba at the invitation of the corresponding Argentine societies. Argentine chairman of the meeting was Dr. Alvaro Bence. The subjects treated were: diagnostic and therapeutic indications of bronchology and esophagology, hospital services of oral endoscopy and oral endoscopy in children.

Correspondence

MEDICAL CONDITIONS IN ALASKA

To the Editor:—The special article on Medical Conditions in Alaska in THE JOURNAL, Oct. 25, 1947, page 500, terminated with a number of recommendations to treat, protect and improve the health of the people of Alaska.

Between 1942 and 1946 I was physician-in-charge at the Point Barrow Hospital and was responsible for the health of the people along the Arctic shore. In 1943 the Kotzebue Hospital and the district it covered was also assigned to me. I then traveled between the two hospitals and had the opportunity to visit every Eskimo village in the two districts more than once during layovers and field trips.

The Special Investigating Committee was accurately informed that in most of the native villages at least 25 per cent of the people had active tuberculosis at any one time. The number of active cases in the territory was estimated at a minimum of 4,000. They recommended that a minimum of one thousand beds be made available for the isolation and treatment of patients with tuberculosis. They suggested immunization with BCG vaccine to reduce the incidence of tuberculosis. However, they made no further recommendations for the care and treatment of the remaining 3,000 persons with active cases of the disease.

I had hoped that they would follow up their description of the congestion in the native homes, which they considered one of the main causes for the tremendous incidence of tuberculosis, with a suitable recommendation. I believe that there is a solution to that problem if sufficient interest and attention could be focused on it.

The best in Eskimo culture, in addition to their fine manners, is exemplified by their hand-sewn fur garments and skin clothing and the making of skin-covered boats. Their homes, however, are simple and designed primarily to provide shelter—there is no privacy or convenience. These are permanent structures. The Eskimo is not a nomad. Permanent villages are established at the best hunting and fishing sites. The Eskimo igloo is really a sod house—seldom larger than 10 by 12 by 6 feet (305 by 366 by 183 cm.). There is generally a short, low, entry way used for storage and the shelter of young or weak dogs in the winter. Light is conveyed through a skylight consisting of a wooden frame 2 feet (61 cm.) square, supporting several bowed rods which project outward and on which sewed strips of walrus gut are stretched. There is a small air vent 2 by 6 inches (5 by 15 cm.) leading through the sod roof. The sod house is built around a frame of wooden posts and beams or whale ribs. Heat is furnished by a small oven, fabricated from a discarded oil drum, or a small iron stove. In the villages in which there has been a strong influence exerted by white men, whalers, traders and gold miners, most of the sod houses have been replaced by the more modern wooden frame house. In a country where the temperature during January and February falls to 45 to 50 degrees below zero, and the velocity of the wind may rise to 50 to 60 miles per hour and continue for days, no more preposterous type of home could have been devised. It proves how easily the Eskimo is attracted to white men's ways and how willing he is to accept them.

At Point Barrow, a community of close to six hundred persons, there is only one sod house which is occupied. All other fifty-five houses are wooden frame structures. Except for about six houses which are larger, nearly all measure 10 feet (305 cm.) wide, 13 feet (299 cm.) long and 7 feet (213 cm.) high. The inner and outer walls are 4 inches (10 cm.) apart. In the spring of 1943, with the aid of a native assistant, I had measured every dwelling at Point Barrow and enumerated the number of inhabitants in each. In some there were as many as fourteen persons. The average was ten persons to a house. The records of this survey are on file at the Point Barrow Hospital. We listed 80 known cases of tuberculosis with active primary and secondary types of infection.

The reason for the congestion was the lack of fuel and food. There was insufficient driftwood; "outside" coal cost $70 per ton; a week's supply of pitch, secured from oil seepages located at Cape Simpson 60 miles (97 kilometers) to the east, required a dog team of at least seven dogs, a hunter's time and effort for five to seven days, and food for himself and the dogs. These could rarely be spared from the more urgent pursuit of hunting. An inadequate supply of pitch from Cape Simpson and coal from outcroppings at Wainwright 100 miles (161 kilometers) to the west was secured during the summer months, when the ice receded from the shore and permitted the whale boats to motor to Cape Simpson and Wainwright. There was no money for the purchase of "outside" coal except by a few more provident families.

Similar conditions prevailed up and down the Arctic coast. At Wainwright, where outcroppings of coal existed, the wooden frame houses and the sod igloos were slightly larger and were inhabited by fewer persons. But at Point Lay, Point Hope, Kivilina, Shishmaref, Deering, Wales, and Kotzebue, conditions were similar to that of Point Barrow. In these villages, except for Kotzebue, sod igloos predominated.

The pioneers who settled the Western Plain states in the last century lived in large, relatively comfortable sod houses—far better than those the Eskimos occupy today. In the Arctic there are millions of acres of tundra out of which to build large commodious sod houses with privacy and with some conveniences.

The Eskimos of the Arctic have entered into a new phase of cultural relations with the white man. Whereas prior to the war they were isolated, their only contact with the outside world being through the government teachers, missionaries, Army Signal Corps operators, the annual freight boat and the pilot of the occasional mail plane, today they are encompassed by the men and machines of the United States endeavoring to build Alaska into a military base. The hunting economy is rapidly being displaced by easier and more assured methods of earning money and purchasing the needed supplies at the trader's store.

The Eskimo has changed his mode of life but not his dwelling. His manual skill, reliability, self effacing manner and congenial nature have made him a much sought-after employee by the Navy oil contractors at Point Barrow, the Alaska Road Commission, the Army engineers, the U. S. Weather Bureau and the Civil Aeronautic Authority. The Eskimos have the money but lack the know-how.

The basic material is underfoot. The Eskimo has the money to purchase the additional materials and fuel. I believe that a capable architect could devise a model modern Eskimo home which would provide several rooms with thick sod walls, privacy and sanitary conveniences, eliminating congestion and reducing the chance for the dissemination of tuberculosis. If this is done, I believe that the care of large numbers of patients with active tuberculosis who will not secure admission to the projected sanatoriums may then be provided at their homes. An effort to solve the problem of the 3,000 remaining cases of active tuberculosis will then have been made.

EDWARD D. SEINFELD, M.D., Middletown, Conn.

To the Editor:—The special article in THE JOURNAL of Oct. 25, 1947, on medical conditions in Alaska contained two statistical items on which further information would be appreciated.

1. The death rate from tuberculosis is quoted as being 359.1 per hundred thousand for 1945-1946. From that figure it is deduced that the total number of cases of open pulmonary

tuberculosis in Alaska approximated 4,500. If we accept the "usual practice of multiplying the number of deaths from tuberculosis by nine to arrive at a conservative figure of open cases" we would arrive at an approximate figure of 3,240, rather than 4,500.

2. According to the article, 69 per cent of all deaths from communicable disease during 1945 were due to tuberculosis. The death rate from other communicable diseases would amount to approximately 155 per hundred thousand. Which communicable diseases contribute to the majority of these deaths?

The report on the tuberculosis problem in Alaska is one of the most alarming ones. The fact that the war-torn countries of Europe show a tuberculosis death rate of even 400 to 500 per hundred thousand is no great consolation. Alaska did not suffer from four years of warfare on its territory, from chronic undernourishment and frank starvation. The housing shortage is undoubtedly critical, but no population shifts like the one seen in Europe has occurred to aggravate this shortage.

Dr. Johannes Holm, the director of the Danish tuberculosis control program, reported last June in San Francisco to the annual convention of the National Tuberculosis Association on the work that the Danish Red Cross has been doing to help stem the rising tide of the white plague in Europe. According to him, teams of Danish doctors and nurses, financed by the Danish Red Cross, have been traveling throughout the war-devastated areas of Europe for the purpose of immunizing tuberculin-negative persons with BCG vaccine and at the same time training native doctors and nurses in the technic of immunization.

It is conceded that in this country BCG vaccination still has not been generally recognized as an effective means of reducing the incidence of tuberculosis. On the other hand, reports from a number of large cities in the Eastern part of the United States tend to confirm the impression that BCG vaccination offers a certain amount of protection.

On page 509 of the article on conditions in Alaska the advisory committee also recommends an "extended immunization program with BCG or a similar method" among the native population of Alaska.

If the Danish Red Cross, drawing its financial support from a population of 4,000,000 persons, has had the courage to undertake such expeditions as those described herein, it is my belief that the American Red Cross or the National Tuberculosis Association, or both, in conjunction with the American Medical Association could sponsor a similar program.

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CHILD ASPHYXIATED BY SULFONAMIDE TABLET

To the Editor:—I saw today death from asphyxiation of a child caused by half a sulfadiazine tablet prescribed by a physician; the tablet became lodged in the larynx. The child, aged 2½ years, was brought to my office soon after she became asphyxiated. Although she was apparently dead, I performed a hurried tracheotomy and removed the softened pieces of tablet and gave artificial respiration, but it was too late. Since the advent of sulfonamide drugs the divided tablets are, no doubt, frequently prescribed for young children. This report is to warn physicians of the danger of administering tablets to young children. Parents should be instructed to crush the divided tablet in a teaspoon and moisten with water. Preferably, one of the sugar lozenges or pleasant-tasting liquid sulfonamide preparations now available should be prescribed.

C. L. HEALD, M.D., Sigourney, Iowa.

Medical Motion Pictures

FILM REVIEWS

Eyes That Hear. 16 mm., black and white, sound, 600 feet (one reel), showing time seventeen minutes. Prepared in 1946 for the Lexington School for the Deaf, New York. Produced by Campus Film Productions, New York. Procurable on loan from Lexington School for the Deaf, 904 Lexington Avenue, New York 21, and the Volta Bureau, 1537 Thirty-fifth Street N.W., Washington, D. C.

The film concerns the problems that confront the parent of a deaf child. Step by step it reveals how these problems are solved in the Lexington School for the Deaf in New York. As one follows the work through into the older age groups, one sees the signs of increasing earnestness of purpose and again is thankful for the absence of that unctuous optimism that mars some films of this sort. Toward the close one actually hears a class of deaf children talking and singing in unison—an amazing achievement.

There must be many persons in the United States to whom this film would be a revelation; young and old can understand what it is about and can catch its urgent message—that a deaf child needs expert help and that there are places where such help can be obtained.

This picture has been produced to provide members of the educational and medical professions as well as the lay public with an introduction to the work being done in schools for the deaf. The photography is good.

Accident Service. 16 mm., black and white, sound, 1,300 feet (one reel), showing time forty minutes. Prepared in 1944 by the British Ministry of Information, London. Produced by Great Britain Instructional Ltd. Procurable on rental or purchase from British Information Service, 30 Rockefeller Plaza, New York 20 or local office.

This film presents an accident hospital and rehabilitation service, depicting the primary and secondary treatment of surgical accidents such as fractures of the spine, the long bones, hands and feet. The detailed management of the patient from admission to the hospital through the various stages, inclusive of the period of rehabilitation conducted in a separate rehabilitation center, are pictured.

The presentation naturally falls under two divisions, namely, the hospital surgical therapy and the management in the rehabilitation center. For example, the progress of a patient with spinal fracture is pictured from the place of injury through all the gradations of surgical care in the hospital and of therapy in the rehabilitation center to his final return to the job, with emphasis on the cooperation of plant physician, hospital surgeon and rehabilitation, welfare and management personnel in restoring the patient to working capacity.

The treatment of various types of fractures such as a fracture of the vertebra with roentgenologic aid and the technic of reducing an open fracture of the tibia is demonstrated in detail. A special and invaluable feature is the inclusion of diagrammatic sketches illustrating the mechanics of setting fractures and grafting skin. Plastic technic is particularly well shown, and the handling of primary surgical shock is emphasized. The extreme importance of early remedial muscular exercises in cases of fracture is stressed.

The film also calls attention to the importance of the psychosomatic aspects of surgical therapy—setting the mind of the patient at rest with respect to recovery of job and economic status and giving him the "will to recover."

The film leaves a clear impression of the activities of a thoroughly modern type of rehabilitation center in which the patients are housed. The fundamental principles of physical therapy are clearly defined and illustrated in the depiction of gymnastic exercises, occupational therapy and recreational exercises. These various aspects are presented in great detail. The rehabilitation center has all the recreational facilities of a service club.

This film is recommended for undergraduate medical students, industrial physicians, orthopedic surgeons, physical training personnel and physical therapy technicians.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Evidence: Admissibility of Results of Lie Detector Test on Defendant and Complaining Witness.—The defendant was convicted of a felonious assault and appealed to the Supreme Court of Kansas.

The defense to the criminal charge was to the effect that the defendant had not assaulted the complaining witness but rather that the complaining witness was caught in the act of stealing one of the defendant's horses and was shot in the resulting struggle. At the first trial the jury was unable to agree and was discharged. Following the first trial, and in compliance with the court's expressed desire, the defendant and the complaining witness submitted to lie detector tests, but there was no stipulation or agreement that testimony might be admitted at a second trial concerning the results of such tests. The tests were made by Phil Hoyt, captain of police in Kansas City, Mo., who testified that he had been conducting tests with the lie detector since 1937. He took this training under Keeler of Northwestern University, who is largely credited with developing the instrument. The witness described the lie detector and its operation as follows: "This instrument is an ordinary blood pressure cuff similar to that used by a physician in taking blood pressure. You place it around the right arm and the pressure from the artery is carried to an attachment that registers with a pen based on a pivot which leaves a graph on paper, being wound by a motor at a rate of 6 inches (15.24 cm.) per minute. Another attachment is an ordinary rubber tube, one end of which is a smaller hose which goes to an attachment that records the respiration on the graph paper by a pen. By respiration I mean breathing of the person taking the test. The object is that theoretically every person who lies deliberately will show some physical reaction, and with most people it is registered by a rising blood pressure and a subconscious block in breathing. The difference in breathing is ordinarily 17 to 19 inhalations a minute, which is usually increased during a five second period." Hoyt was then permitted not merely to testify whether in his opinion the tests indicated, generally, truthfulness or falsification on the part of the defendant and the complaining witness but to give his interpretation of their answers on the essential issue of the case—whether the complaining witness' story or the defendant's story was the true one; whether the complaining witness was kidnapped, deliberately shot in the foot and under threats to his life forced to sign the written confessions, or whether the complaining witness went to the defendant's farm after dark and the defendant, on discovering him attempting to steal a horse, shot toward the ground with resultant injury to the complaining witness.

The practical effect of the admission of this testimony, said the court, was to constitute a mechanical device—as reported by the operator—a sort of witness in absentia on the question of the defendant's guilt or innocence. In no case cited by the defendant or found in our own research, the court stated, has a court of last resort sanctioned the admission of such testimony.

Cogent reasons in support of this attitude of the courts readily suggest themselves, the court continued. In the first place, the vital function of cross examination would be impaired. The operator, appearing as a witness to report and interpret the results of the test, might be questioned as to his qualifications, experience, methods and the like, and that is about all. But the machine itself—conceding the comparatively high percentage record as to accuracy and reliability claimed for it—escapes all cross examination. Many innocent but highly sensitive persons would undoubtedly show unfavorable physical reactions, while many guilty persons, of hardened or less sensitive spirit, would register no physical indication of falsification. Of course, the trained operators understand this and proceed on the basis of a large percentage of error. But it seems too subtle a task of evaluation to impose on an untrained jury. We are not ready to say, concluded the court, that the lie detector has attained such scientific and psychologic accuracy, or its operators such sureness of interpretation of the figures on a dial, that the testimony here in question was competent, over objection, for admission to a jury holding the fate of the defendant in its hands.

About twenty years have elapsed, said the court, since the admissibility of a lie detector test was first passed on in a reported case. The only reported decision of which we are aware holding such a test admissible is *People v. Kenny*, 1938, 3 N. Y. S. (2d) 348. In all other reported cases the courts have rejected such tests, generally on the ground that their reliability has not yet been sufficiently established. And even the Kenny case, in which an expert was permitted to testify concerning a test made on the defendant, is no authority to support the admissibility of a test on a complaining witness. In 1946, in an article in the Boston University Law Review, Fred E. Inbau, professor of law at Northwestern University and an associate of Dr. Keeler, says: "A number of trial courts have admitted in evidence the testimony of lie-detector examiners as to their interpretation of test records in instances where, prior to the test, counsel for both litigants agreed and stipulated that the test results could be used in evidence without objection on the part of the party adversely affected thereby. . . . But in the absence of such pre-test agreements and stipulations, the test records and the examiner's interpretation thereof have been held inadmissible as evidence by every appellate court which has had occasion to consider the matter, for the very understandable reason that the test had 'not yet gained such standing and scientific recognition among physiological and psychological authorities as would justify the courts in admitting expert testimony deduced from the discovery, development, and experiments thus far made.'"

Accordingly the Supreme Court concluded that the trial court erred in admitting the lie detector evidence and reversed the judgment of conviction.—*State v. Lowry, 185 P. (2d) 147 (Kan., 1947).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARD OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL Jan. 24, page 280.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I & II.* Various centers, June 21-23. *Part II.* Various centers, April 26-27. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* New York, April 12-15. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written. Group B.* Various centers, Feb. 16. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* San Francisco, April. Chicago, June. Final date for filing application is Feb. 1. *Written.* Oct. 18. Final date for filing application is June 1. Asst. Sec.-Treas., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application is Feb. 1. Sec., Dr. W. J. German, 310 Cedar St., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral. All Groups. Part II.* Washington, D. C., May 16-22. Final date for assignment is April 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Baltimore, May 20. Chicago, Oct. 6. *Written.* Various centers, Jan. 1949. Final date for filing application is July 1, 1948. Sec., Dr. S. Judd Beach, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, June 16-19. Final date for filing application is Feb. 1. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Philadelphia, March 8-10. Final date for filing application is March 1. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis, Mo.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in April and November of each year in the home town of applicants. Sec., Dr. Robert H. Ivy, 1930 Chestnut St., Philadelphia.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* Washington, D. C., May 13-15, 1948. Final date for filing application is Feb. 15. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, June 1948. Final date for filing application is March 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

Annals of Internal Medicine, Lancaster, Pa.

27:487-682 (Oct.) 1947

Problem of Neurotic Patient. W. C. Menninger.—p. 487.
*Streptomycin in Treatment of Meningitis: Report of 27 Cases Treated at Boston City Hospital. T. F. Paine, R. Murray, A. O. Seeler and M. Finland.—p. 494.
*Pleuropulmonary Tularemia. H. J. Morgan.—p. 519.
*Nitrogen Mustard as Therapeutic Agent for Hodgkin's Disease, Lymphosarcoma and Leukemia. M. M. Wintrobe, C. M. Huguley Jr., Margaret T. McLennan and L. P. de Carvalho.—p. 529.
Development of Basophilic Inclusion Bodies in Myeloma Cells After Stilbamidine Treatment. I. Snapper and B. Schneid.—p. 541.
New Drugs of Value in Treatment of Epilepsy. F. A. Gibbs.—p. 548.
Insulin Resistance. A. R. Axelrod, S. Lobe, J. M. Orten and G. B. Myers.—p. 555.
Relative Importance of Dietary Sodium Chloride and Water Intake in Cardiac Edema. L. W. Gorham, E. Lester, A. V. Wolf and H. H. Shultz.—p. 575.
Prognosis of Syphilitic Aortic Insufficiency. G. G. Reader, B. J. Romeo, B. Webster and W. McDermott.—p. 584.
Post-Partal Heart Disease. J. P. Melvin Jr.—p. 596.
Hereditary Polycystic Kidney. J. F. Cannon.—p. 610.

Streptomycin in Meningitis.—According to Paine and associates streptomycin has been used in the treatment of 27 cases of meningitis at the Boston City Hospital. There was 1 death among 16 cases due to Hemophilus influenzae and 2 deaths among 8 cases due to other gram-negative bacilli. The deaths occurred in 2 patients in whom treatment with streptomycin was begun late in the disease. The third fatality was associated with the development of a streptomycin resistant strain of Pseudomonas aeruginosa during treatment. Two of 3 patients with tuberculous meningitis are living, and their disease appears to be arrested. The results in these and similar cases reported by others seem to justify the following conclusions: 1. Streptomycin is the only agent now available which may arrest the progress of tuberculous meningitis. 2. Streptomycin is the most effective single agent in the treatment of meningitis due to gram-negative bacilli, including H. influenzae. The authors note 8 additional cases of meningitis treated with streptomycin since the completion of this report. They include additional cases caused by H. influenzae, by Escherichia coli communis and Klebsiella pneumoniae, also additional cases of tuberculous meningitis. Two of these cases, 1 caused by an organism of the coli group and 1 caused by K. pneumoniae, terminated in death.

Pleuropulmonary Tularemia.—Morgan presents histories of selected cases from the Vanderbilt University Hospital material and reports 15 additional cases of pleuropulmonary tularemia treated with streptomycin in Veterans Administration hospitals. The recognition of tularemic infection with or without pulmonary involvement does not pose a problem when the typical primary ulcer and regional buboes are present. In the absence of these lesions the clinical picture is obscure. The author found that more than half of the pleuropulmonary tularemic infections presented themselves as instances of obscure pulmonary infections or masqueraded as cases of primary atypical pneumonia of unknown etiology. In such circumstances the clinician is seriously handicapped even when the possibility of tularemic infection is considered and diagnostic tests for its presence are employed, for the demonstration of Pasteurella tularensis in culture or by mouse inoculation is time consuming and dangerous, and diagnostic agglutinins do not appear in the patient's blood until the end of the second or during the third week of infection. Thus patients with severe tularemic infections may die before an accurate diagnosis can be established by these methods. Streptomycin has been found to cure pleuropulmonary tularemia, which in the prestreptomycin era had a mortality rate of from 20 to 40 per cent. A therapeutic trial with streptomycin may save life in an infection which sometimes kills before a diagnosis can be made. Administration of streptomycin does not inhibit the subsequent appearance of diagnostic agglutinins. A therapeutic trial with streptomycin is indicated in critically ill patients suspected of having severe primary atypical pneumonia or other forms of virus pneumonia, when the illness is of less than two weeks' duration and when it occurs in a region where tularemia is endemic.

Nitrogen Mustard in Hodgkin's Disease, Lymphosarcoma and Leukemia.—The nitrogen mustards (beta-chloroethylamines) differ from the wartime mustard gas only in that nitrogen replaces sulfur. The biologic effects of the nitrogen mustards are almost identical with those of radiant energy. Wintrobe and his associates have used methyl bis (beta-chloroethyl) amine hydrochloride (nitrogen mustard) in 28 patients with Hodgkin's disease, 11 with lymphosarcoma, 26 with leukemia and 12 with miscellaneous diseases. An infusion of isotonic sodium chloride solution is started, and its smooth running into the vein is assured. To 10 mg. of dry white crystalline hydrochloride salt of the mustard is added 10 cc. of sterile isotonic sodium chloride solution. The salt dissolves promptly, and the calculated dose of solution is withdrawn into a sterile syringe. This is administered immediately by injecting it through the rubber tubing of the saline infusion. A salutary effect on lymph nodes, fever, splenomegaly and various clinical symptoms, similar to that produced by roentgen irradiation, was observed in many patients with Hodgkin's disease, lymphosarcoma and leukemia. Nitrogen mustard has produced remissions in several patients with Hodgkin's disease who were considered to be roentgen resistant. Toxic manifestations of nausea and vomiting were observed in most patients. Nitrogen mustard therapy almost invariably resulted in a decrease in leukocyte count with lymphocytopenia and granulocytopenia. This was often accompanied by a decrease in red cells and platelets. Subsequent to the initial decrease in blood elements, an increase in red cells even with complete disappearance of anemia was the result in those patients who responded favorably. Leukopenia and thrombocytopenia likewise disappeared. Nitrogen mustard offers certain advantages as compared with roentgen irradiation. These include ease of administration, effectiveness, at times, in patients resistant to roentgen therapy, and, rarely, a better tolerance for nitrogen mustard than for irradiation. Ultimately, however, nitrogen mustard, like irradiation, has proved ineffective in many cases.

Archives of Neurology and Psychiatry, Chicago

58:391-532 (Oct.) 1947

Disseminated Encephalomyelitis Experimentally Produced by Use of Homologous Antigen. L. R. Morrison.—p. 391.
Psychosurgery During 1936-1946. W. Freeman and J. W. Watts.—p. 417.
Penicillin in Treatment of Neurosyphilis. B. Dattner, S. S. Kaufman and E. W. Thomas.—p. 426.
Electroencephalogram in Porencephaly. J. P. Murphy and J. S. Garvin.—p. 436.
*Electroencephalogram in Poliomyelitis. B. L. Pacella, C. W. Jungeblut, N. Kopeloff and Lenore M. Kopeloff.—p. 447.
Effect of Crossing Nerves to Antagonistic Limb Muscles in Monkey. R. W. Sperry.—p. 452.
Innervation of Choroid Plexus. Maria Tsuker.—p. 474.
Clinicopathologic Aspects of Parkinsonian States: Review of Literature. J. W. Heath.—p. 484.

Electroencephalogram in Poliomyelitis.—Pacella and his associates studied electrophysiologic alterations of the brain during the course of poliomyelitis. Definite or consistent electroencephalographic changes which might indicate abnormal electrocortical activity were not observed prior to the onset of fever or paralysis in monkeys given intracerebral injections of strains of simian poliomyelitis virus. Abnormalities in the electroencephalogram appeared during the paralytic stage and became more conspicuous with the progression of symptoms. The electroencephalographic changes consisted chiefly in a progressive increase of slow activity, disappearance of alpha rhythm, a relative increase in the amount of fast activity and

a lowered voltage output. Electroencephalographic abnormalities were not noted in guinea pigs given either intracerebral or peripheral injections of murine poliomyelitis virus in the presence or in the absence of paralytic symptoms. Of 17 patients convalescent from poliomyelitis, all of whom had severe residual paralysis, 2 exhibited definite electroencephalographic abnormality and 5 showed a borderline disturbance. The remaining 10 patients had normal electroencephalograms.

Cincinnati Journal of Medicine

28:575-636 (Sept.) 1947

Clinical Use of Anticoagulants. E. V. Allen.—p. 575.
Psychosomatic Conference of Cincinnati General Hospital. M. Rosenbaum and F. T. Kapp.—p. 582.

28:637-716 (Oct.) 1947

Surgical Treatment of Hypertension. R. H. Smithwick.—p. 637.
Newer Diagnostic Methods in Heart Disease: Their Application in Clinical Practice. A. Iglauer.—p. 657.

Connecticut State Medical Journal, Hartford

11:889-960 (Nov.) 1947

Management of Complications of Diabetes. Elaine P. Ralli.—p. 892.
Acute Appendicitis in Myelogenous Leukemia: Case Report. B. B. Landry and J. O'L. Nolan.—p. 897.
Tularemia: Case Report; Recovery with Use of Streptomycin. H. A. Archambault.—p. 899.
Placenta Accreta as Cause of Concealed Antepartum Hemorrhage. C. G. Barnum, F. Hartman and F. Brundage.—p. 900.
*Mineral Oil—A Health Hazard. Florence A. Browne.—p. 903.
The Way Out—Postwar Medical Temptations and Solutions. P. J. White.—p. 905.
Progress in Medicine—From Horse Power to Jet Power. B. B. Robbins.—p. 910.
Hartford Medical Society. E. J. Whalen.—p. 915.

Mineral Oil, a Health Hazard.—Browne points out that in spite of warnings that the ingestion of mineral oil has a deleterious effect on human beings, many persons have continued to take it by mouth, in the belief that its only actions are those of softening the feces and lubricating the intestines. Notable among the constant users of mineral oil are pregnant women and women wishing a substitute for vegetable oils in reducing diets. During the war, because of the shortage of oils of vegetable origin, salad dressings made with mineral oil instead of vegetable oils became more numerous on market shelves, and new uses for it were found, such as the preparation of popcorn, salted nuts, doughnuts, croquettes and potato chips. Mineral oil interferes with the absorption of vitamins and minerals, with normal physiologic processes of the intestinal tract and with anal hygiene. Animal experiments have shown that the belief that mineral oil is not absorbed by the intestines is untenable. Physicians not only should not recommend mineral oil but should warn patients against its use. Only in this way will its consumption be reduced. More consideration should be given to the causes of constipation and their removal.

Illinois Medical Journal, Chicago

92:201-256 (Oct.) 1947

Pathologic Anatomy of Diabetes Mellitus. E. T. Bell.—p. 215.
Methacrylic Resin Implant for Sunken Upper Lid Following Enucleation. H. S. Sugar and H. J. Forestner.—p. 219.
*Tularemia in Illinois. H. E. McDaniels.—p. 224.
Biliary Fistulae Due to Gallstones, with Report of 2 Cases. J. R. Cochran and R. E. Dolkart.—p. 228.
Problems of Epidemic Ringworm of Scalp. S. J. Zakon and A. L. Goldberg.—p. 232.
Therapy of Allergy: Facts and Fancies. S. M. Feinberg.—p. 234.
Use and Abuse of Physical Therapy in Treatment of Arthritis. E. F. Traut.—p. 238.
A New Sign in Diagnosis of Minimal and Moderate Ascites. L. Cardon.—p. 239.

Tularemia in Illinois.—According to McDaniels, 95 per cent of the cases of tularemia in Illinois are acquired by skinning or cleaning wild rabbits. During the ten years ending with 1945, there was an average of about 185 reported cases per year in Illinois. However, the number of cases has ranged from 55 to 485. Cook County, with over half the population of the entire state, reports about 10 per cent of the cases. Wild rabbits sold in the markets of Chicago and suburbs come principally from Missouri, Iowa, Illinois, Kansas and the Dakotas. Many of the Chicago cases among market men, housewives, etc., are attributable to these rabbits. Other Chicago patients received their infection while hunting rabbits in southern counties of Illinois and in neighboring states. About 85 per cent of all reported cases have been ulceroglandular infections. Approximately 10 per cent have been reported as being of the typhoidal variety. The remaining 5 per cent are made up of oculoglandular and glandular infections. In the typhoidal type of tularemia the incubation period tends to be longer by about one week than in the ulceroglandular cases. The shortest duration was sixteen days, the longest three hundred and sixty days. The most effective treatment of tularemia consists of the administration of streptomycin in adequate amounts. The prophylactic measures recommended by the author include among others the use of rubber gloves by persons engaged in dressing wild rabbits or in performing necropsies on laboratory animals; employment of immune persons for dressing wild rabbits or conducting laboratory experiments; thorough cooking of meat of wild rabbits, and avoidance of raw drinking water in areas where the disease prevails among wild animals.

Journal of Experimental Medicine, New York

86:357-437 (Nov.) 1947

Studies on Mechanism of Adaptation of Influenza Virus to Mice. G. K. Hirst.—p. 357.
Comparisons of Influenza Virus Strains from Three Epidemics. G. K. Hirst.—p. 367.
Effect of Sulfhydryl Groups on Pneumonia Virus of Mice (PVM). M. Volkert and F. L. Horsfall Jr.—p. 383.
Studies on Lung Tissue Component Which Combines with Pneumonia Virus of Mice (PVM). M. Volkert and F. L. Horsfall Jr.—p. 393.
*Transmission of Epidemic Gastroenteritis to Human Volunteers by Oral Administration of Fecal Filtrates. I. Gordon, H. S. Ingraham and R. F. Korns.—p. 409.
Demonstration of One-Step Growth Curves of Influenza Viruses Through Blocking Effect of Irradiated Virus on Further Infection. W. Henle, Gertrude Henle and Evelyn B. Rosenberg.—p. 423.

Transmission of Epidemic Gastroenteritis.—Gordon and his associates say that numerous outbreaks of gastroenteritis occurred in New York state institutions during the fall and winter of 1946-1947. The disease was characterized by a sudden onset, by profuse diarrhea, usually accompanied by vomiting, and by a lack of fever. Symptoms ordinarily persisted for about three days. Bacteriologic examinations failed to reveal agents known to cause enteric disease, and postmortem investigations failed to indicate the nature of the etiologic agent. A search was made for a nonbacterial pathogen. Since preliminary animal experiments were unsuccessful, human volunteers were utilized. The illness was reproduced and transmitted in series in volunteers, and the responsible agent was shown to be filterable. Oral administration of stool suspensions or throat washings induced the disease, but inhalation of nebulized throat washings did not. Volunteers who were fed material from the third embryonated egg passage likewise remained asymptomatic.

Journal of Urology, Baltimore

58:295-395 (Nov.) 1947

Renal Salvage. A. I. Dodson.—p. 295.
*Nephroptosis Producing Duodenal Symptoms. R. E. Van Duzen—p. 304.
Ureteral Diverticulum: Classification of Literature and Report of an Authentic Case. O. S. Culp.—p. 309.
Diverticulum of Ureter: Review of Literature and Report of 2 Additional Cases. J. G. Pratt, H. Q. Gahagan and J. L. Fischman.—p. 322.
Vesical Diverticula: Clinical Study with Special Reference to Treatment. H. M. Spence and S. S. Baird.—p. 327.
Congenital Diverticulum of Male Urethra. W. G. Knox.—p. 344.
Urethroceles in Urology. D. K. Rose.—p. 349.
Vesico-Vaginal Fistula. B. W. Turner.—p. 359.
Syphilis of Prostate: Report of Case and Review of Literature. E. Crowley and E. Thomas.—p. 367.
Re-Emphasis on Four Simple Cystoscopic Rules for a Successful Transurethral Prostatic Resection. H. S. Browne.—p. 372.
Flow Meter for Transurethral Surgery. G. O. Baumrucker.—p. 375.
*Bone Changes and Variations in Skeletal Metastases Due to Diethylstilbestrol and Orchiectomy During Treatment of Cancer of Prostate. C. A. Wattenberg.—p. 378.
Perineal Testicle. A. B. Cecil.—p. 384.
Use of Estrogenic Hormone in Plastic Operations on Penis. V. Vermooten.—p. 391.

Nephroptosis Producing Duodenal Symptoms.—Van Duzen presents histories of 3 patients who had been treated for duodenal ulcer and who were relieved by division of fibrous bands running from the hilus of the right kidney to the second

portion of the duodenum. The author believes that these bands represent not an anatomic structure or ligament but a condensation of fibers from Gerota's fascia, which run from the hilus of the kidney to the duodenum. In cases 1 and 2 it was easy to understand how the dropping of the kidney, which was demonstrated by roentgenogram, would produce traction on the duodenum. In case 3 the kidney was fixed in one position and the band constricted the lumen of the duodenum. After section of the band, the duodenum became normal in shape, as proved by later roentgenograms.

Estrogens and Orchiectomy in Prostatic Cancer.—Wattenberg cites investigations which show that repeated injections of estrogens over long periods cause a condition of generalized hyperossification, which fits in with the roentgenologic observations and microscopic sections of skeletal metastases due to cancer of the prostate gland, before and after treatment with diethylstilbestrol and bilateral orchiectomy. The author shows in roentgen ray films and high power and low power views of bone tissue that estrogens can inhibit metastatic carcinoma not only by changing the carcinomatous cells but also by hyperossification about the regressed tumor cells. Views of carcinomatous prostatic tissue before and after treatment with diethylstilbestrol demonstrate that diethylstilbestrol and bilateral orchiectomy can cause a regression of the metastatic carcinoma of the prostate and a regression of the primary carcinoma of the prostate.

Laryngoscope, St. Louis

57:633-682 (Oct.) 1947

Treatment of External Otitis: III. Use of Vehicles and Antibiotics in External Auditory Canal in Vitro Studies. B. H. Senturia and J. A. Doubly.—p. 633.
Use of Antibiotics in Treatment of Bacterial Infections. W. B. Wood Jr.—p. 657.
*Changing Concepts of Sinusitis. F. J. Putney.—p. 664.
Plasmocytoma: Report of Case. J. B. Costen.—p. 671.

Changing Concepts of Sinusitis.—According to Putney surgical treatment of sinusitis has largely been replaced by medical management. The emphasis is on restoration rather than removal or destruction of diseased tissue. The sulfonamide drugs and the antibiotics have changed the treatment of sinusitis. In longstanding suppurative sinusitis the membrane becomes fibrotic and little benefit results from use of the sulfonamide compounds or penicillin. Sinusitis is classified as allergic, mechanical or bacterial. Allergic cases require primary attention to the allergic diathesis; those due to mechanical blockage are relieved by simple surgical procedures, and early bacterial sinusitis responds to penicillin. Penicillin is equally valuable in treating the complications of orbital cellulitis and osteomyelitis of the skull. Surgery can often be avoided when penicillin is given early, but in chronic osteomyelitis surgical drainage is usually needed in addition to the drug.

New England Journal of Medicine, Boston

237:651-682 (Oct. 30) 1947

*Diagnostic and Therapeutic Value of Liver Biopsies with Particular Reference to Trocar Biopsy. W. Volwiler and C. M. Jones.—p. 651.
*Renal Damage Following Intravascular Hemolysis. E. L. Burwell, T. D. Kinney and C. A. Finch.—p. 657.
Granuloma Inguinale with Perianal Involvement: Report of Case. J. Berkowitz.—p. 665.
"Folic Acid" Pteroylglutamic Acid and Related Substances. F. Sargent II.—p. 667.
Hepatoma, with Invasion of Cystic Duct and Metastasis to Third Lumbar Vertebra.—p. 673.
Meningioma of Spinal Cord.—p. 676.

Trocar Biopsy of Liver.—Volwiler and Jones state that needle or trocar biopsy of the liver has advantages over other methods. When properly performed, it causes little discomfort and, if a fairly uniform pathologic process is present, provides a satisfactory sampling of tissue from deep within the hepatic substance. They have performed 234 needle biopsies with 0.5 per cent mortality. Of the total number, 216 provided sufficient tissue for adequate histologic appraisal; in 79 cases the biopsy was essential to an accurate clinical diagnosis. Aspiration liver biopsy will furnish the following practical information: correct differentiation of extrahepatic and intrahepatic biliary obstruction when clinical and laboratory data are inconclusive; exact diagnosis of the type of diffuse intrahepatic disease; determination of the particular phase of a known subacute or chronic hepatitis; indications for therapy not obtainable from clinical and laboratory examinations, and accurate evaluation of therapeutic regimens in certain types of chronic hepatic disease. Needle aspiration liver biopsy has proved a useful and safe measure for making exact diagnoses and for studying the abnormal physiology of disease of the liver.

Renal Damage Following Intravascular Hemolysis.—The observations reported by Burwell and his associates are concerned with the medical management of the anuric patient and with the functional and anatomic reversibility of the renal lesion produced. A housewife aged 29, who had had an abortion during the week prior to admission, recovered from the anuria that followed massive hemorrhage but succumbed three months later to homologous serum hepatitis. During the intervening period the renal function showed steady improvement, as evidenced by clinical and laboratory tests. Necropsy offered a unique opportunity to correlate the residual anatomic lesions with the clinical picture. The fact that the renal function tests improved until the time of death suggests eventual complete recovery. Necropsy showed little residual damage to the kidney.

New Jersey Medical Society Journal, Trenton

44:439-477 (Nov.) 1947

*Combined Antigens in Treatment of Rheumatoid Arthritis. P. J. Warter, D. A. Donio and S. Horoschak.—p. 441.
*Pruritus Ani: Biochemophysiologic Entity. H. E. Bacon and C. E. Hardwick.—p. 446.
Benign Paroxysmal Peritonitis: Report of 2 Cases. T. S. Heineken.—p. 451.
Role of Private Practitioner in Venereal Disease Case Finding. W. A. Brumfield.—p. 453.
Control of Epidemic Diarrhea by Decentralization of Infants. I. J. Wolf.—p. 456.
Unstable Colon. S. B. Kaplan.—p. 458.

Treatment of Rheumatoid Arthritis.—Warter and his associates emphasize that the treatment of rheumatoid arthritis should be directed against the etiologic factors rather than the affected joints. Mental and physical rest; maintenance of adequate nutrition, control of pain and eradication of obvious foci of infection are essential to the successful treatment of rheumatoid arthritis. On the premise that foci of infection, streptococci, and their toxins or toxic products play some role in the causation of rheumatoid arthritis, the authors decided to incorporate into their therapeutic regimen the use of streptococcus-staphylococcus-vaccine-toxin toxoid combined antigen. Clinical results with this combined antigen have been as favorable as, and in a number of patients more favorable than those obtained with gold therapy. If the action of gold therapy is to alter the biologic activity of tissue sensitized to infection, then the combined antigen is much safer. The antigen proved effective in arresting and controlling rheumatoid arthritis in 71.1 per cent of the 90 patients observed from two to four years.

Pruritus Ani.—Bacon and Hardwick suggest that pruritus ani may be due to a disturbance in the acid-base balance which resulted in a change occurring in the bacterial flora, this in turn raising the p_H of the rectal mucosa. This alkaline reaction has been constantly present in the majority of the cases of pruritus studied by the authors. It is their opinion, based on previous histopathologic determinations, that pruritus ani is a form of chemical dermatitis varying in its skin changes. They have been using since 1946 a medical routine aimed at reducing the p_H of the rectal mucosa. This includes an acid-ash diet and glutasin capsules (a form of glutamic acid hydrochloride in combination with pepsin). Gelatin suppositories which contain beta-lactose are used. The diet reduces the p_H and the glutasin, which acts as hydrochloric acid when administered orally, aids in this process. The lactose suppositories tend to prevent the seepage of rectal discharges of a high p_H during the night. Following evacuations they advise the use of cotton pledgets, using a boric saturated solution to remove secretions. The area is kept thoroughly dry with boric powder. Improvement is evident following the judicious use of this regimen. The authors tabulate observations made on 125 cases of pruritus ani.

New York State Journal of Medicine, New York

47:2239-2366 (Nov. 1) 1947

Effect of Anesthesia and Surgery on Patients with Pulmonary Tuberculosis. W. M. Parke Jr., E. R. Loftus and H. F. Bishop.—p. 2285.
Difficulties in Diagnosis and Treatment of Lesions of Pyloric Antrum. H. L. Segal, J. S. Watson Jr. and T. B. Steinhausen.—p. 2292.
Anal Incontinence. S. T. Ross.—p. 2299.
Complications Peculiar to Ulcerative Diseases of Colon. N. D. Smith. —p. 2304.
Carbon Tetrachloride Poisoning: Report of 7 Cases with 2 Deaths. I. Gray.—p. 2311.
Evaluation of Penicillin in Topical Therapy. J. L. Miller, J. J. Rodriquez and A. N. Domonkos.—p. 2316.
Ragweed Dermatitis (Oral Desensitization). B. J. Slater, J. L. Norris and N. Francis.—p. 2322.

Surgery, Gynecology and Obstetrics, Chicago

85:547-674 (Nov.) 1947

Applied Anatomy of Femoral Vein and its Tributaries. E. A. Edwards and J. D. Robuck Jr.—p. 547.
Lymph from Liver and Thoracic Duct: Experimental Study. J. C. Cain, J. H. Grindlay, J. L. Bollman and others.—p. 559.
*Gelatin Nephrosis: Renal Tissue Changes in Man Resulting from Intravenous Administration of Gelatin. O. K. Skinsnes.—p. 563.
Sodium Pentothal Anesthesia for Selected Vaginal Obstetrics. A. L. Dippel, R. J. Helman, C. E. Wolters and others.—p. 572.
*Andrologic Endocrinology: Correlation of Clinical Symptoms, Urinary Hormone Excretion and Testicular Cytology. J. W. Goldzieher and E. C. Hamblen.—p. 583.
Comparative Study of Thromboangiitis Obliterans in White and Negro Patients. H. A. Davis and L. D. King.—p. 597.
Report on Use of Harris Tube. R. E. Herrera, J. B. Millet and G. H. Lawrence.—p. 604.
*Diverticula of Duodenum and Jejunum with Report of New Technical Procedure to Facilitate Their Removal and Discussion of Their Surgical Significance. H. Mahorner and W. Kisner.—p. 607.
Carcinoma of Larynx: Methods and Results of Treatment. G. B. New, F. A. Figi, F. Z. Havens and J. B. Erich.—p. 623.
Monteggia Fractures: Analysis of 25 Consecutive Fresh Injuries. F. M. Smith.—p. 630.
Neurilemmoma of Pharynx. C. E. Koop, H. E. Jordan and R. C. Horn. —p. 641.
Comparative Hematologic Findings in Normal, Splenectomized and Spleen-Transplanted Dogs. A. L. Copley, P. L. Stefko and Janet Naylor.—p. 646.

Gelatin Nephrosis.—Skinsnes reports on postmortem examinations of 23 patients who received gelatin intravenously in quantities ranging from 100 to 17,600 cc. with widely varying intervals between the final injection and the death of the patient. The gelatin, derived from pig skin, was given in an 8 per cent solution in isotonic sodium chloride solution, usually in doses of 800 cc. The patients died as a result of medical and neoplastic disease or from complications of therapeutic surgical measures. The renal lesion produced by gelatin is compared with that of sucrose nephrosis. Gelatin nephrosis is a reversible change occurring within half an hour after its intravenous administration and disappearing within one hundred and twenty hours following the last injection. Studies of the effect of the renal lesion on renal function are inconclusive. In 1 patient diuresis developed and in another oliguria following intravenous administration of gelatin. Caution is suggested in patients with previous renal impairment. Three cases are reported which suggest gelatin as a potential precipitating factor in coronary occlusion and vascular thrombosis in the presence of circulatory disturbances and vascular disease.

Urinary Hormone Excretion and Testicular Cytology.—Goldzieher and Hamblen report 8 patients selected to illustrate discrepancies between clinical evidence of androgenic activity, urinary hormone excretion and testicular histology. Increased numbers of Leydig cells were associated with low or high 17 ketosteroid excretion, or with normal or high gonadotropin excretion. Decreased numbers of Leydig cells were associated with very low, low, normal or high 17 ketosteroid excretion and with low or high gonadotropin excretion. The authors confirm the observation of Heller and Nelson that there is no quantitative correlation between elevation of gonadotropic excretion and 17 ketosteroid output. Clinical evidence of hypoandrogenism was observed in the presence of low or high 17 ketosteroid excretion. Eunuchoid habitus was present with high, normal or low gonadotropin excretion or with increased or decreased numbers of Leydig cells. A large penis was noted with low, normal or high 17 ketosteroids and a small penis with high normal 17 ketosteroids. Evidence of feminization was observed with high normal 17 ketosteroids and increased numbers of Leydig cells with low normal 17 ketosteroids and with low 17 ketosteroids and few Leydig cells. Gynecomastia was observed in the presence of increased or greatly decreased numbers of Leydig cells, and yet with normal sized penis. It was seen with normal or low gonadotropin excretion or with normal or low 17 ketosteroid excretion. Hypertrophy or hyperplasia of Leydig cells cannot be regarded as indicative of increased or even of normal secretory activity. It is possible that studies of mitochondria and Golgi apparatus, as well as the use of perfected histochemical technics, may provide adequate cytologic criteria of endocrine cellular activity.

Intestinal Diverticula: Surgical Removal.—Mahorner and Kisner state that duodenal and jejunal diverticula occur in from 1 to 2 per cent of patients who have roentgenographic studies made for gastrointestinal symptoms. The prevailing opinion was that they are relatively innocuous, but they frequently are responsible for disabling symptoms. Medical measures such as a bland diet and recumbency on one side after each meal are acceptable only for patients whose physical condition precludes operative treatment. Surgery is indicated if the symptoms are sufficiently severe. When duodenal diverticula are large enough to cause residual pooling of barium, removal or inversion is indicated. Jejunal diverticula are much less common than diverticula of the duodenum and are much more difficult to diagnose preoperatively. They may cause severe symptoms. Their surgical removal results in cure. The authors describe a new technic of pumping up the duodenum with air to show diverticula which may be hidden, particularly those protruding into the head of the pancreas or into the retroduodenal area. This new procedure should insure their discovery at the operating table and thus facilitate their removal. A group of 6 cases are reported, in each of which operative intervention was performed and the patient was relieved of his symptoms.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

55:573-624 (Nov.) 1947

*Indications for Thyroidectomy for Hyperthyroidism. G. Crile Jr.—p. 573.
Some Observations on Exophthalmos. F. F. Rundle.—p. 578.
Maternal and Infant Mortality: Comparative Study Covering Period of Twenty Years, Based on Records of Hospital of Good Samaritan at Los Angeles, California. R. H. Fagan.—p. 584.
Preservation of Threatened Pregnancy with Particular Reference to Use of Diethylstilbestrol. G. Rosenblum and E. Melinkoff.—p. 597.
Lipoma of Ileum Causing Ileo-Ileal Intussusception in an Adult. L. B. Sherry.—p. 604.
Case of Thrombophlebitis and Allergy. A. J. Lesser.—p. 607.
Esophageal Duplications of Mediastinal Cysts of Enteric Origin. J. C. Jones.—p. 610.
New Infant Tracheotomy Tube. W. F. Goff.—p. 618.

Hyperthyroidism.—According to Crile, thiouracil proved to be an effective means of preparing patients with severe hyperthyroidism for thyroidectomy, but its toxicity was too high to render it acceptable for general use as a definitive treatment. Propylthiouracil is relatively safe, and, although not so effective as thiouracil, it still affords an excellent means of controlling hyperthyroidism without undue danger of side effects. The author used propylthiouracil in 218 patients. The dosage used, 200 to 300 mg. daily, is not always sufficient to maintain a remission. Judging from the prompt recurrences which have taken place in patients who have of their own accord discontinued treatment after a few months of control, incidence of remissions will not be as high as had been anticipated. If the patient is cooperative and can be observed by a physician who is familiar with the structure of the thyroid and the pharmacologic action of the antithyroid drugs, treatment can be extended over long periods. When the patient is uncooperative or cannot be observed periodically, it is preferable to perform a thyroidectomy. Patients with small or moderate sized diffuse goiters with mild or moderate hyperthyroidism, patients with recurrent hyperthyroidism and patients whose life expectancy is short, regardless of the type of goiter, may safely be given a trial on medical management for a year or more. If they respond favorably and prefer medical treatment, this may be continued indefinitely. If they respond poorly or desire surgery, a subtotal thyroidectomy should be performed.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:641-680 (Oct. 25) 1947

*Etiology of Steatorrhea. A. C. Frazer.—p. 641.
*Some Problems of Tropical Sprue. D. A. K. Black and L. P. R. Fourman.—p. 645.
Shock in Obstetrics. W. A. Scott.—p. 647.
*Breast Feeding in Erythroblastosis Fetalis. I. A. B. Cathie.—p. 650.
Residual Subacute and Chronic Prostatitis After Penicillin and Sulfonamide Therapy in Acute Gonorrhea. F. C. Bourgault du Coudray.—p. 651.
Thiopentone-Nitrous-Oxide-Oxygen Anesthesia with Curare for Head and Neck Surgery. J. G. Bourne.—p. 654.

Etiology of Steatorrhea.—Frazer says fat absorption may be divided into three phases: an intraluminar phase, during which the fat undergoes preparatory changes in the intestinal lumen; an intracellular phase in which the fatty material passes through the intestinal cell and a distributive phase when the fat is dispersed from the intestine by various pathways into the body. Defective lipolysis, as in atrophic pancreatitis or defective bile salts as in biliary obstruction, is to be considered as a possible defect of fat absorption in the intraluminar phase. Interference with water and electrolyte metabolism, whether due to adrenal cortical insufficiency or to other causes, defective phosphorylation and defective transport from the cell may be the possible defect of fat absorption in the intracellular phase. Experiments demonstrated that in the distributive phase of fat absorption fatty acids mainly pass up the portal vein to the liver, while triglycerides absorbed largely in particulate form take the lymphatic route and pass by the thoracic duct into the systemic circulation. The proportion of fatty material which passes by these two alternative routes might be considerably varied without any great change in the total quantity of fat absorbed. The proportion of fat which is absorbed in particulate form may be reduced with a corresponding increase in fatty acid absorption. Such a mechanism would provide the flexibility which is apparent in cases of defective absorption. The main factors which seem to be concerned in changes in the distributive phase, apart from the obstruction to the lymphatic pathway, are the p_H in the intestinal lumen and the composition of the dietary triglyceride.

Tropical Sprue.—Black and Fourman measured the total output of fat in the stools of 28 patients with early tropical sprue. By subtraction from the dietary fat (65 Gm. and 95 Gm., respectively, daily), they arrived at the total amount absorbed; for this, when expressed as a percentage of the dietary fat, the term percentage fat absorption is suggested. The fat absorption determined by this method ranged from 50 to 85 per cent, while normal persons taking a mixed diet containing 50 to 100 Gm. of fat daily will absorb over 90 per cent of the dietary fat. Evidence suggests that there is a fairly general impaired absorption in sprue and that fat malabsorption has been first observed only because its effects on the stools are more obvious. In therapeutic trials with nicotinic acid and riboflavin in large doses the patients failed to show improvement either in their clinical state or in fat absorption. With large doses of a crude liver extract given parenterally there was rapid gain in weight and well-being and improvement in the character of the stools. In spite of this the percentage of fat absorption did not change detectably in several weeks of liver therapy and thereafter improved only slowly as the patient's general condition approached normal. When yeast extract in a dose of 15 to 20 Gm. daily was given to patients who were receiving liver treatment, there was some improvement in fat absorption within the first twelve day period. Yeast treatment is more convenient for the patient than frequent injections of crude liver extract. A number of patients with sprue became acutely ill with salt deficiency dehydration associated with watery diarrhea; in such patients diarrhea must be controlled with sulfaguanidine and parenteral liver, and their diet should also be supplemented with moderate amounts of salt.

Breast Feeding in Erythroblastosis Fetalis.—Cathie obtained the fasting gastric contents from 20 infants between the ages of 1 week to 1 year. Equal volumes of gastric secretion and serum with Rh antibody titer were incubated together for one hour at 37 C. (98.6 F.). No fall in titer was found in any case, indicating that Rh antibodies are not readily destroyed by the gastric juice. Twelve Rh-positive infants, suffering from such conditions as inoperable spina bifida, were fed for a complete day with high titer serum. There was complete failure to demonstrate any antibody absorption. The direct Coombs test was done daily on an infant with erythroblastosis. On the day when the test became negative and for the subsequent twenty-four hours only high titer serum was fed, and again no sensitization of the red cells occurred and antibody could not be demonstrated. The same investigation was carried out again, but on the day the Coombs test became negative the infant was put on breast milk containing an anti-Rh titer of 32. The infant's red cells did not become resensitized, and antibody was not otherwise demonstrated in the serum. In these studies complete antibody was used. The series was completed by repeating the observations on infants with hemolytic disease but using incomplete or blocking antibody. Again evidence of absorption was not observed. It is concluded that weaning infants with hemolytic disease because the maternal milk contains antibodies is not justified.

Edinburgh Medical Journal

54:401-464 (Aug.)1947

Tuberculous Infection and Disease of Lung in Childhood. C. McNeil.—p. 401.
Pulmonary Mycosis. T. G. Brown.—p. 414.
Nonspecific Urethritis of Virus Etiology. P. N. Meenan.—p. 423.
Bacteriemia, Factor of Prognosis in Pneumonia. K. S. Alstad.—p. 427.
Prevention of Mastitis: Nursing Problem. Edith C. Thomas.—p. 436.
*Treatment of Acute Puerperal Mastitis. J. S. Jeffrey.—p. 442.
Clostridium Welchii Infection of Pleural Cavity. R. W. P. Johnson.—p. 447.
Some Impressions of American Medicine. J. L. Henderson.—p. 449.

Treatment of Acute Puerperal Mastitis.—Jeffrey reports 50 cases of acute puerperal mastitis that occurred among 3,500 puerperal women. The 40 treated with penicillin all responded. Of the 5 treated with sulfathiazole 3 responded satisfactorily, in 1 there developed an abscess that required incision and 1 did not respond until penicillin was given. Of the 5 treated with fomentations 4 responded and the other one required treatment with penicillin. Penicillin was given to 30 patients by means of injections at intervals of three hours of 25,000 units (200,000 units per day) for seven days; in the other 10 patients penicillin was given every twelve hours in doses of 100,000 units. Equally good results were obtained with the less laborious method of two daily injections. The author concludes that penicillin should be continued for at least three days. If the cellulitis does not rapidly settle, the possibility of a resistant staphylococcus infection must be considered and a sulfonamide drug should be administered; otherwise, penicillin alone is sufficient. Fomentations are not advisable because they macerate the nipple. The only local treatment needed is firm support in the form of a many tailed binder with shoulder bands. Pain in the breast, headache and elevation of temperature are early signs of mastitis.

Transactions Royal Soc. Trop. Med. and Hyg., London

41:93-141 (Sept.) 1947. **Partial Index**

Studies on Genus Shigella. L. M. González, P. Morales-Otero and J. E. Perez.—p. 93.
Sprue and Celiac Disease in Tropical Africa. M. Gelfand.—p. 109.
*Serologic Tests for Syphilis in Treated Plasmodium Falciparum Malaria. M. G. Nelson.—p. 127.
Epidemic of Louse-Borne Relapsing Fever in Kenya. P. C. C. Garnham, C. W. Davies, R. B. Heisch and G. L. Timms.—p. 141.

Serologic Tests for Syphilis in Malaria.—Serologic tests for syphilis have been carried out on 200 patients under treatment for malaria due to Plasmodium falciparum. Three flocculation tests were employed by Nelson in parallel—Ide, Kahn and Meinicke—and the false positive results obtained were approximately 3 per cent. Malarial false positives do not persist long after the period of clinical activity—one month in treated patients and two months in untreated ones. Serologic follow-up for two months after discharge from the hospital following malarial treatment should permit a differential diagnosis. Kahn verification tests by the differential heat method failed to confirm the nonspecific nature of the reaction in

malaria. It is considered that even the Richardson potentiation test gives equivocal results with positively reacting serums from patients with malaria. If there is careful control to exclude syphilis and yaws, malaria causes fewer false positive results with modern flocculation methods than was at first assumed.

Nordisk Medicin, Gothenburg

35:1691-1738 (Aug. 15) 1947. **Partial Index**

Psychoses in Mentally Defective. J. Ravn.—p. 1691.

Hospitalstidende

Solitary Lung Cysts: Symptomatology, Diagnosis and Treatment. E. W. Andersen.—p. 1703.

Fractionation of Serum Protein According to Henriques and Clausen Method and with Methanol. J. Bock.—p. 1705.

Extractum Filicis in Treatment of Tapeworm with Fatal Outcome (Oil-Aspiration Pneumonia). J. V. Jørgensen.—p. 1707.

Norsk Magasin for Lægevidenskapen

Blast Injury. A. Jakobsen.—p. 1709.

*Respirator Treatment of Respiratory Paralysis in Acute Poliomyelitis. V. Gaustad.—p. 1712.

*Thirteen Poliomyelitis Patients Given Respirator Treatment. B. Ingebrigtsen.—p. 1718.

How Can the United States Become Better Acquainted with Norwegian Medicine? Axel Strøm.—p. 1721.

Hygeia

Experiences in Field of Plastic Surgery in Urology. A. Frumkin.—p. 1727.

Respirator Treatment in Acute Poliomyelitis.—Gaustad says that 41 of the 61 patients with poliomyelitis treated in the Sahlin respirator in Ullevål Hospital from 1936 to 1945 died in the respirator and 7 died later; 13 are living. Of the 27 female patients, 15 were over 18 years of age and 5 of these were pregnant. Twenty-three deaths were due to circulatory failure, 13 to pulmonary complications. In 9 cases both factors were responsible. Of the 27 patients with respiratory paralysis of the bulbar type, 25 died. In respiratory paralysis the autonomic nervous system is usually affected. Artificial respiration and failure in regulation of the circulation by the autonomic system are probably both important factors in the circulatory failure. Electrocardiographic studies of patients during respirator treatment showed extremely high and in part pointed P waves in leads 2 and 3. Respiratory paralysis is more frequent in older patients. The prognosis in respirator treatment seems to be more favorable for the younger patients. Even though the mortality in patients given respirator treatment is as high as 80 per cent, a sufficient number of respirators is indispensable for every hospital which is to treat poliomyelitis in the acute stage.

Thirteen Poliomyelitis Patients Given Respirator Treatment.—From a follow-up of the 13 patients still living after respirator treatment of 61 patients from 1936 to 1945 (V. Gaustad) Ingebrigtsen concludes that about half of the poliomyelitis patients who survive respirator treatment retain their ability to work.

Presse Médicale, Paris

55:717-732 (Oct. 25) 1947

New Variety of Tubercle Bacillus "Mycobacterium Tuberculosis Var. Muris." P. Hauduroy.—p. 717.

Cesarean Section. H. Vermelin.—p. 717.

Charles Ruppe's Disease: Fibrous Osteitis of Maxillaries. L. Lebourg and M. Henault.—p. 718.

*Epidemiologic and Practical Interest in Natural Antagonistic Effect of Staphylococcus on Loeffler's Bacillus. P. Lesbre and A. Merle.—p. 719.

*Bacteriostatic and Bactericidal Properties of Fatty Acids of Cod Liver Oil and of Its Distillate. J. Solomidès.—p. 719.

Antagonistic Effect of Staphylococcus on Loeffler's Bacillus.—Lesbre and Merle noted an absence of cases of diphtheria in the maternity ward in Limoges during an epidemic recurrence of diphtheria in this town, while in previous years diphtheria had spread from this ward to other locations. Not a single carrier of Loeffler's bacillus could be demonstrated among the infants and nursing personnel. Staphylococcus albus was isolated from swabs in 96 per cent of this group. This observation induced the authors to paint a twenty-four hour gelose culture of staphylococcus on the tonsils of 4 persons who had been chronic carriers of Loeffler's bacillus for three months. This application was repeated three to four times at forty-eight hour intervals. Loeffler's bacillus disappeared within one week, and in 2 of these carriers symptoms of a partial paralysis of the soft palate subsided rapidly. The same favorable results were obtained in an additional 60 persons who had been carriers of Loeffler's bacillus for shorter periods. The patients were advised not to eat and drink for four hours after the painting. There were only 4 failures. The antagonistic effect of staphylococcus on Loeffler's bacillus was much less apparent in a liquid than in a solid medium. It is the growth on the surface which seems to play the primary part and allows for lytic diastasic action demonstrated by alcoholic extraction. Selected, nonpathogenic Staph. albus in a fresh culture at the height of its vitality should be employed, since its ability to spread over a surface is the essential factor in its action.

Bacteriostatic and Bactericidal Properties of Cod Liver Oil.—Solomidès observed that bacteriolysis and simultaneous appearance of an abundant cyanophilous substance resulted from the introduction of 1 cc. of vegetable, animal or mineral oil in the culture of tubercle bacilli on potatoes. The pathogenic power of the oleolyzed cultures varied, depending on the chemical constitution of the oil, but tuberculous oleolysis resulted from all kinds of oils. Cod liver oil definitely killed the lyzed tuberculous cultures, while peanut oil and paraffin oil did not. Under certain conditions of p_H and with well determined concentrations the alkali soaps of the fatty acids contained in cod liver oil were capable of inhibiting the growth of Staphylococcus aureus in mildly alcoholized broth in considerable dilutions (1:9,000,000). Pneumococci and streptococci proved to be even more sensitive to these substances, since inhibition of their growth could be obtained in even higher dilutions of 1:9,000,000,000 and 1:90,000,000. The tubercle bacillus was killed by this product in glycerinated broth in dilutions of 1:50,000. Thus the antituberculous principle contained in cod liver oil may be identified reasonably with one or several of the free fatty acids of this oil or of those liberated in the culture by the lipase of the tubercle bacillus itself. Further experiments showed that the growth of tubercle bacilli may be controlled with an alcoholic emulsion of distillates of cod liver oil ranging from 1:6,000 to 1:10,000. It is concluded that the fatty acids of cod liver oil are active in considerable dilution against pneumococci, staphylococci and tubercle bacilli and that the distillate of this oil is a strong bacteriostatic agent against the tubercle bacillus.

Revista de la Asociación Méd. Argentina, Buenos Aires

61:609-660 (Aug. 30) 1947. **Partial Index**

*Cervical Herniation of Lung. A. V. Di Ció, J. M. Remolar and G. A. Lista.—p. 611.

*Bronchial Hamartoma: Three Cases. O. A. Itoiz, R. I. Latienda and A. J. Murray.—p. 614.

Cervical Herniation of Lung.—The condition is rare. The subject of this report by Itoiz and associates was a man aged 31, in whom there developed attacks of pain similar to angina pectoris on the left side. A painless herniation appeared in the left supraclavicular region the day after the first attack. Diagnosis of cervical herniation of the lung was made on roentgen examination of the chest, which showed uniformly transparent lung tissue, including the herniated apex. There were roentgenologic signs of chronic pulmonary emphysema of the bronchogenic type. The ribs were normal. The author believes that the congenitally increased volume of the lung, in the presence of pulmonary emphysema, was the causal factor of the herniation. Operation was contraindicated because of pulmonary emphysema, which favors recurrence of herniation.

Bronchial Hamartoma.—Three cases of bronchial hamartoma were found in a total number of 11,859 necropsies performed at the Institute of the Faculty of Medicine of Buenos Aires (a frequency of 0.25 per thousand). There were no symptoms during life. In the first case the condition was accompanied by two accessory pancreases and a Meckel diverticulum and suggested a common disgenetic origin. In the third case the hamartoma was endobronchial and pediculated and presented the appearance of an adenoma. The 3 cases showed benign macroscopic and microscopic structure and an organoid structure.

Book Notices

Meals for Millions. Final Report of the New York State Joint Legislative Committee on Nutrition, 1947. Legislative Document (1947) No. 61. Paper. Pp. 213, with illustrations. State Senator Thomas C. Desmond, Chairman, New York State Joint Legislative Committee on Nutrition, 94 Broadway, Newburgh, New York, 1947.

Few functions of government are "more important than assuring that citizens have available adequate diets" says Senator Desmond; yet in the state of New York there is no official nutrition program—nor does the nation have one. Senator Desmond and his committee have made a careful study of foods and food needs as they relate to the maintenance of health. Their recommendations are based on their own studies and on consultations with a large group of medical and nonmedical nutritionists. In conclusion they reach a logical decision, namely, that the nation and the state needs a strong nutrition program now. With this as a premise, Senator Desmond's committee proposes a plan of action that is precise, workable and needed. This report deserves the thoughtful consideration of all those concerned with the health of the nation.

Preoperative and Postoperative Care. By William J. Tourish, M.D., F.A.C.S., Demonstrator of Surgery and Chief Clinical Assistant in Surgery, Jefferson Medical College and Hospital, Philadelphia, and Frederick B. Wagner Jr., M.D., Instructor in Surgery and Assistant in Surgery, Jefferson Medical College and Hospital. Foreword by Thomas A. Shallow, M.D. Cloth. Price, $6. Pp. 338, with 87 illustrations. F. A. Davis Co., 1914-1916 Cherry St., Philadelphia 3, 1947.

This timely book is well arranged, covering general preoperative care, general postoperative care and specific preoperative and postoperative care. Under general preoperative care the authors consider age, operative risk, nutritional preparation, care of the bowels, fluid and electrolyte balance, preanesthetic medication, choice of anesthesia and psychotherapy. Under general postoperative care are discussed care of the uncomplicated case as well as the complicated cases, which they consider under the heading of immediate, early and late postoperative complications. Due consideration is given to the recent advances in therapy such as the use of blood and blood derivatives, protein hydrolysates, vitamins, sulfonamide drugs and antibiotics.

They deal with specific preoperative and postoperative care for all types of operations arranged according to systems such as neck, chest, intrathoracic, liver and gallbladder. Special chapters are devoted to the urologic, neurosurgical and gynecologic patients.

This book is concise, easily readable and well illustrated. It should serve as a handy reference for the busy surgeon, for the operator remote from the large medical centers, the busy resident and the intern. One may question the emphasis placed on the responsibilities of the intern—many of which should be assumed by the surgeon in charge of the patient. This book should occupy a place in every hospital library.

Anatomy and Physiology for Students of Physiotherapy, Occupational Therapy and Gymnastics. By C. F. V. Smout, M.D., M.R.C.S., L.R.C.P., Assistant Professor of Anatomy, University of Birmingham, and R. J. S. McDowall, M.D., D.Sc., Professor of Physiology, University of London, King's College. Second edition. Cloth. Price, $8. Pp. 470, with 318 illustrations. William Wood & Co., Mount Royal & Guilford Aves., Baltimore 2, 1947.

This textbook deals with anatomy and physiology from the point of view of the student in physical medicine and occupational therapy. The volume provides an approach to anatomy with an emphasis on skeletal and neuromuscular structures that is deficient in many of the shorter textbooks, which attempt to combine anatomy and physiology. The section on anatomy consists of 333 pages with 298 illustrations. The illustrations have been carefully selected and are superlatively reproduced. Many are in color. The functional and mechanical considerations of the skeletal and neuromuscular systems are emphasized. Basic principles of bodily mechanics are presented in two special chapters, one entitled "Levers and Leverage" and the other, "Muscles in Action." However, the volume is not designed as a textbook on kinesiology.

The section on physiology includes only 111 pages. Basic principles of physiology are presented in a clear and concise manner. The usual physiology course for physical and occupational therapy students would require a more complete coverage of physiology than this book provides. However, this section correlates important physiologic facts with the fields of physical and occupational therapy. Muscular activity, physiologic effects of exercise, massage and heat are briefly summarized. A brief and interesting glossary indicates the Greek and Latin derivations of terms. The index is complete and well organized. This book will be a valuable aid to the student in physical therapy and occupational therapy. However, because of its brevity it should not be considered as an adequate textbook of either anatomy or physiology. The physiatrist as well as other physicians interested in a brief, basic, functional approach to anatomy and physiology will welcome this book.

Concise Anatomy. By Linden F. Edwards, Ph.B., Professor of Anatomy, Ohio State University, Columbus, Ohio. Cloth. Price, $5.50. Pp. 548, with 324 illustrations. The Blakiston Company, 1012 Walnut St., Philadelphia 5, 1947.

To those familiar with Dr. Edwards' "Anatomy for Physical Education" the present volume will not be a stranger. "Concise Anatomy" is, in effect, a second edition with a change of title. Rearrangement and amplification, with the exception of a section on general microscopic and developmental anatomy, have not been extensive. Thus former users may anticipate a volume of the same quality and method of presentation as before with the added advantage of the new section which, though brief, outlines its subject matter clearly and is well illustrated for a work of this size.

Whether this book will appeal to a teacher of nonmedical anatomy depends on his interests and emphasis. As a compromise between regional and systematic anatomy, the general ordering of the details is good and might well be copied by the larger reference books. However, some will certainly feel that the role of functional interpretation has been slighted, especially since this is a textbook intended for physical education and physical therapy majors, among others. For example, although the joints of the foot are succinctly described, discussion of the functional significance of the talocalcaneonavicular complex is not undertaken. Walking as a coordination of muscle and joint activities of trunk, pelvis and legs is neglected.

A Textbook on Pathology of Labor, the Puerperium and the Newborn. By Charles O. McCormick, A.B., M.D., F.A.C.S., Clinical Professor of Obstetrics, Indiana University School of Medicine, Indianapolis. Second edition. Cloth. Price, $8.50. Pp. 514, with 272 illustrations. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1947.

The author has added several new sections, including the Caldwell-Moloy pelvic classification, conduct of the third stage of labor, Burns's technic in breech presentation, the author's technic in external version, conduct of impacted shoulder, anticoagulants in the treatment of thrombophlebitis, cardiac disease, eclampsia and diabetes mellitus complicating labor and the puerperium, sudden death during labor and the puerperium, early rising and religious requirements and restrictions of the Catholic Church. Many new illustrations have been added, and the aphorisms have been increased to seventy-five.

The Braxton Hicks version which is advocated as a method of treating placenta previa, many obstetricians believe should be given up entirely. Likewise the Credé maneuver should be condemned in treating postpartum hemorrhage. The author recommends external version under deep surgical ether, but most obstetricians who employ this procedure prefer to do it without anesthetic.

The introduction of the anterior blade of the Kielland forceps is shown as advocated by Kielland, but it is much less dangerous to insert the anterior blade by making it "wander" into place, as with most other forceps. Too many illustrations are devoted to monsters, especially to rare ones. In the section on monsters there are nine photographs, and in the special chapter on malformations there are four more photographs. Likewise, fourteen illustrations seem too many to devote to destructive operations. The proprietary names "pituitrin" and "ergotrate" are retained in this edition instead of the nonproprietary names, posterior pituitary injection and ergonovine maleate, respectively. The word fundus is used where corpus is meant, as in the legend for figure 107.

In spite of these minor defects the book contains excellent advice, preaches conservative obstetrics, is well written and

abundantly illustrated. The book is not intended to replace the complete textbooks of obstetrics but simply to cover pathologic obstetric conditions. In this aim the author has succeeded admirably.

Dental Caries: Its Etiology, Pathology, Clinical Aspects and Prophylaxis. By Bernhard Gottlieb, M.D., D.M.D., LL.D., Professor of Oral Pathology and Dental Research, Baylor University College of Dentistry, Dallas, Texas. Cloth. Price, $10. Pp. 262, with 229 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1947.

This monograph on dental caries is based on the special pathology of the tissues concerned. The author rightly states, "A correct knowledge and understanding of normal structures is a fundamental requirement for the study of their pathological changes. If some error exists in the concept of the interpretation of normal conditions, then the concept of the interpretation of the pathology will be erroneous. The lines between normal structure, pathology, and clinical consideration should never be sharp and definite. The student of normalcy may easily overlook something. His mistake may appear in the clinical and pathological considerations, and be perpetuated and magnified there." In spite of this the author has advanced a highly theoretic and controversial opinion, indicating that Staphylococcus aureus produces dental caries because yellow pigmentation is frequently associated with dental caries. Naturally this is an assumption that will be contested by a majority of workers in this field.

The text includes an extensive study of the development and structure of the enamel and the problems of the formation of secondary dentine. The part which is devoted to prophylaxis of caries and the discussion about fluorine deserve study by both dentists and physicians. Illustrations are magnificent and establish Gottlieb as one of the great dental technicians of all time.

Charles-Édouard Brown-Séquard: A Nineteenth Century Neurologist and Endocrinologist. By J. M. D. Olmsted, M.A., Ph.D., D.Sc., Professor of Physiology, University of California, Berkeley, California. Publications of the Institute of the History of Medicine, The Johns Hopkins University. Third Series: The Hideyo Noguchi Lectures, Volume V. Cloth. Price, $3. Pp. 253, with 2 portraits. The Johns Hopkins Press, Homewood, Baltimore 18; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, 1946.

Here are three lectures given at Johns Hopkins University maintained by a fund contributed in 1929 by the late Dr. Emanuel Libman and now known as the Hideyo Noguchi Lectureship. The writing is clear but not especially distinguished in its literary quality. The furor created by the announcement that an extract of testicular tissues would rejuvenate was from a journalist's point of view a high spot in Brown-Séquard's career. His actual scientific contributions to endocrinology deserve proportionately far more space.

Practical Chemistry for Medical Students. By William Klyne, M.A., B.Sc. With a foreword by G. F. Marrian, D.Sc., F.R.S., Professor of Chemistry in Relation to Medicine, University of Edinburgh, Edinburgh. Cloth. Price, $6. Pp. 460, with illustrations. William Wood & Co., Mt. Royal & Guilford Aves., Baltimore 2, Maryland, 1946.

This is largely a laboratory manual with some theoretical discussion based on elementary courses given to medical students at the University of Edinburgh. The text is divided as follows: some fundamental scientific ideas, practical methods, general and physical chemistry, inorganic chemistry and organic chemistry—the latter including some compounds of biologic importance. Many phases of these branches of chemistry and many individual products are touched on briefly but with little elaboration, which was the declared intention of the author. A sentence or two is added to explain the medical value of each product.

Over de acute en "chronische" koolmonoxyde vergiftiging. [Door] Dr. J. R. Borst. [Acute and chronic Carbon Monoxide Poisoning.] Paper. Pp. 152, with illustrations. A. W. Sijthoff's Uitgeversmaatschappij N.V., Leiden, 1945.

An English summary gives the main results of this Dutch monograph on carbon monoxide poisoning, whose manifestations and complications, acute and chronic, are described on the basis of a thorough study of clinical cases. The quantitative method of estimating carbon monoxide-hemoglobin worked out by C. L. Harders was used in the work. The monograph will be of interest to students of carbon monoxide poisoning.

Entwicklungs-Geschichte des Krankheitsbegriffes. Von Dr. Emanuel Berghoff. Band I, Wiener Beiträge zur Geschichte der Medizin, herausgegeben von Dr. Emanuel Berghoff. Second edition. Boards. Price, $5. Pp. 201. Wilhelm Maudrich, Spitalgasse 1B, Wien IX/2; Distributors in U. S. A.: Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1947.

The first edition of this work was published in 1945. The fact that this second edition has followed so rapidly might indicate that there is still much interest in medical history among the physicians of wartorn Europe or that this work is particularly interesting. As a matter of fact, Berghoff's survey is excellently balanced. He covers the history of ancient medicine adequately, and the account is readable. But the particular value of his contribution is to be found in his analysis of the period after 1700 A. D. As might be anticipated, he presents the work of the Vienna school and its great contribution in both clinical and didactic medicine in considerable detail, but he by no means neglects the other centers of activity. In this first volume of what will presumably form a series of historical essays, very recent trends are not discussed, a natural consequence of the isolation of the war period. Within these limitations the work is a worth while addition to the field of historical medicine.

Surgery of the Ambulatory Patient. By L. Kraeer Ferguson, A.B., M.D., F.A.C.S., Professor of Surgery, Graduate School of the University of Pennsylvania, Philadelphia. With a section on Fractures by Louis Kaplan, A.B., M.D., F.A.C.S., Associate in Surgery, University of Pennsylvania. Second edition. Fabrikoid. Price, $10. Pp. 932, with 645 illustrations. J. B. Lippincott Co., 227-231 S. Sixth St., Philadelphia 5, 1947.

This book fulfils its purpose as an integrated picture of office surgery from diagnosis and treatment to equipment. The author has avoided successfully that difficult term, minor surgery. The procedures described can be carried out in a well equipped office. Whether this is the wisest course in a number of instances may be doubted, but their feasibility is unquestioned. As a matter of fact, the definition of an ambulatory patient is rapidly changing. With the present shortage of hospital beds the field is certainly enlarging.

Aside from the doubtful value of sulfonamide compounds used locally, there is little to be criticized and much to be praised. The illustration of "how to do a rectal examination" is fascinating—the importance and simplicity of this diagnostic means is too frequently slighted. The general practitioner can well benefit from this book.

Histopathology of the Ear, Nose and Throat. By Andrew A. Eggston, B.S., M.D., Director of Laboratories, Manhattan Eye, Ear and Throat Hospital, New York, and Dorothy Wolff, A.B., M.A., Ph.D., Research Investigator, Endaural Hospital, New York City, Fellow in Research, Harvard Medical School. Cloth. Price, $18. Pp. 1080, with 533 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1947.

This work, performed with obvious zeal and skill, commands the admiration of all at first sight. There are more than 1,000 pages devoted to the histopathology of the ear, nose and throat, with comments on related anatomy and embryology. There are twenty-eight plates. Fifteen are in full color. Hundreds of black and white illustrations, beautifully executed, and an extensive bibliography are included.

Discussion of this volume in detail is superfluous; the authors have accomplished their task in an eminently satisfactory manner. Otolaryngologists and others in related fields will use this work with real pleasure for years to come.

Inorganic Chemistry. By W. Norton Jones, Jr., Professor of Chemistry, Colorado State College of Agriculture and Mechanic Arts, Fort Lewis Branch, Hesperus, Colorado. Cloth. Price, $4.25. Pp. 817; 49, with 247 illustrations. Blakiston Company, 1012 Walnut St., Philadelphia 5, 1947.

The necessity for the physician to understand atomic structure, radioactivity and related phenomena has been repeatedly emphasized; here these facts are presented simply with a clarity and logical development that are exceptional.

Unlike most other books on inorganic chemistry, this one throughout its text introduces the elements "with the purpose of associating the accompanying changes in properties with the structural changes that take place from atom to atom." The result is actually an elementary textbook on physical chemistry as well as inorganic chemistry.

Any physician would be justified and amply repaid in reading at least chapters 2, 4, 5, 6 and 35.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EDEMA OF FEET DURING BUS TRIPS

To the Editor:—A woman patient develops edema of the feet and ankles during prolonged bus trips. The swelling is much less on train rides of two days' duration. She has a slight systolic murmur and a fibroid of the uterus of the size of a baseball, no other pathology. Would you give the reason for this edema? M.D., Ohio.

ANSWER.—The majority of ambulatory patients with edema of the ankles do not have any cardiac disease. A listing of other causes, most of which concern difficulty in the local circulation in the legs dependent on poor veins, overweight and inactivity, can be found in an article by Foote and associates (The Clinical Significance of Bilateral Edema of the Lower Extremities, *Am. J. M. Sc.* **199**:512, 1940). From the data given here it seems unlikely that heart disease is responsible in the case cited. If the heart has not been enlarged and there has been no important dyspnea, the edema is to be ascribed to other cause than cardiac. From the statement that there is "no other pathology" it is unlikely that kidney disease, hypoproteinemia or myxedema plays any role either. There is evidently no other generalized disease process that can be easily identified. To sit or stand for a long time in bus or train would favor edema in a person with faulty leg veins; the longer the trip the greater the amount of such edema.

INJURY TO THE SKIN AND EPITHELIOMA

To the Editor:—A male patient, 35, came into my office May 27, 1947, with a quarter-sized well defined lesion, elevated, infiltrated and erythematous. The center of this area was occupied by a pea-sized verrucous growth. A biopsy of material taken from the edge of the lesion revealed a beginning prickle cell epithelioma, confirmed by a second biopsy. The patient states that on or about April 10, 1947 he was struck by a chip of hot steel while working. He reported to his first-aid station immediately, and a dressing was applied. The area not only failed to heal but continued to increase in size. Several physicians were consulted and several cauterizations were performed, but the lesion continued to increase in size. The question that I would like to pose concerns the time relationship between the trauma and the epithelioma. The patient saw me six weeks after trauma, and the biopsy report of prickle cell epithelioma was present. Can trauma cause an epithelioma in such a short period of time? M.D., Connecticut.

ANSWER.—Theoretically a causal relation between the trauma and the cancer in this case cannot be excluded. Neither can one exclude a potential or preexisting cancer at the site of the trauma. When one considers the frequency of injuries to the skin in daily life without development of cancer, it becomes difficult to accept a causal relationship. Assuming the existence of a causal relation, the writer is unaware of any clinical evidence to indicate the time necessary for the development of cancer following trauma in man.

ASPHYXIA OF THE NEWBORN

To the Editor:—Please discuss asphyxia of the newborn. Recently I have had the anesthetist give oxygen as the head or breech is being delivered and continue the oxygen until the baby is pink. The cord is not tied until pulsations cease, unless there is evidence of hemorrhage. Is it good practice to administer oxygen to the mother for two minutes before the baby is delivered by cesarean section? If the infant can be delivered without cyanosis, isn't it much better than tying the cord immediately and pumping mucus or other secretions into the lungs while administering oxygen. The secretions are supposed to be removed, but this is not always accomplished. W. R. Moore, M.D., Florence, Ala.

ANSWER.—There is good experimental evidence that the establishment of extrauterine respiration is not the cataclysmic event that it has been pictured. Respiratory movements begin early in pregnancy and continue throughout intrauterine life. They are shallow and occur at irregular intervals but are sufficiently strong to move amniotic fluid in and out of the lungs. Any factor which decreases fetal oxygenation will decrease the frequency of these respiratory movements or stop them altogether for a period of time. Analgesic and anesthetic agents likewise depress intrauterine respiratory activity for varying periods, depending on the drug used. At delivery, oxygenation through the placental circulation stops but the respiratory movements fill the lungs with air and the extrauterine respiratory pattern develops. Any depression of the intrauterine respiratory movements interferes with the transition to normal vigorous breathing and results in asphyxia.

Asphyxia of the newborn is thus the result of anoxia during the latter part of labor or during delivery. This may be the result of depression of intrauterine respiratory movements by sedative drugs and anesthetic agents or the result of any condition which interferes with placental circulation, such as cord entanglements, partial placental separation, prolonged labor or difficult operative interventions. Increased oxygenation artificially supplied during the latter part of labor and delivery should decrease anoxia, thereby improving the transition from intrauterine to extrauterine respiration.

ALBUMINURIA AND PREGNANCY

To the Editor:—A woman aged 23 was found in a routine examination to have consistently a 2 to 4 plus albuminuria with a few casts and a specific gravity over 1.020 and at times 1.028. The blood count is normal, the blood pressure 100/70. She is asymptomatic. Intravenous pyelograms reveal a good concentration of the dye. Concentration and emptying of the pelves are equal. The right pelvis is slightly larger than the left. There is a slight ptosis of the right kidney, with a sharp bend in the ureter a third of the distance from the pelvis to the bladder. She had scarlet fever at the age of 5. Several years ago she was kept in bed for "one summer" by a physician, the reason being unknown. She has one child aged 2½ years. During that pregnancy she was "quite sick" during the early months and "felt fine" during the last two months except for swelling of the feet and legs. Labor at term was spontaneous. Her physical condition is satisfactory except for the kidney condition. Should she become pregnant again? If so would there be any reason for early induction of labor or cesarean section to prevent damage to the kidneys? She is anxious to have more children. What is the consensus concerning the induction of labor during the last trimester because of toxemia of pregnancy? Is the induction of labor preferable to cesarean section? What would be the advised method to induce labor in these cases? Is induction of labor or cesarean section preferred in a normal pregnancy with slightly diminished measurements? What statistics afford one procedure the choice above the other? M.D., Kentucky.

ANSWER.—From the information presented it cannot be established that this patient suffers from actual nephritic damage. An orthostatic albuminuria can well account for the variable proteinuria. Orthostatic albuminuria is particularly suspect because of the demonstrated ptosis of the right kidney and slight hydronephrotic dilatation of the right renal pelvis. Certainly comparison of early morning urine (secreted when the patient is recumbent) with that secreted when the patient is erect and/or active is indicated. In orthostatic albuminuria, urine secreted with the patient recumbent will be free or nearly free of protein; urine secreted during activity, especially walking, may be heavily albuminous. Knowledge as to the quantity of protein lost each day is also desirable in estimating nutritional requirements. If such a test should reveal great variation in protein loss correlated to posture and activity, it might be most worth while to obtain separate specimens of urine from each side by ureteral catheterization after a strenuous walk to determine whether the protein is coming from both kidneys or only from the right.

An orthostatic albuminuria is not a contraindication to additional pregnancies. The patient's vulnerability to hypertension can be determined by application of the cold pressor test, first described by Hines and Brown and applied to analysis of the renal vascular problems of obstetrics by Dieckmann and Michel (Dieckmann, W. J., and Michel, H. L.: *Arch. Int. Med.* **55**:420 [March] 1935. Hines, E. A., Jr., and Brown, G. E.: *Proc. Staff Meet., Mayo Clin.* **7**:332 [June 8] 1932; Hines, E. A., Jr.: *Am. Heart J.* **19**:408 [April] 1940).

It is impossible to predict the desirability of early induction of labor in future pregnancies. Frequent antepartum observation should be an adequate guide. The appearance of hypertension during pregnancy is a more significant warning than albuminuria; preexistent nephritis exacerbated by pregnancy is a progressive disorder with a relatively poor prognosis and considerably increased fetal mortality if permitted to continue to full term. Abruptio placentae is a common complication. Hypertension is the most useful criterion of hazardous intoxication. Anemia is also of the greatest importance: future antepartum care should include frequent observations of the blood count and liberal nutritional supplementation to keep the hemoglobin content near optimal levels.

The choice between induction of labor and cesarean section depends largely on factors not stated in the query: pelvic measurements, ease of delivery of the first child and the like. In most instances of nephritis and/or hypertension complicating late pregnancy, conservative medical induction with castor oil and quinine and/or rupture of the bag of waters usually suffice. Cesarean section is indicated in primiparous patients who fail

to respond to conservative measures and who have a long, hard and undilated cervix, a viable baby and intact membranes. Pituitary injection, if administered at all, must be given cautiously because of the hazard of inducing a sharp rise in arterial tension. When any cephalopelvic disproportion exists, the administration of pituitary injection before delivery of the infant is contraindicated. For further discussion of the purely obstetric aspects of the problem, any of the standard textbooks on obstetrics should be consulted.

EFFECT OF "BENADRYL" ON PREGNANCY

To the Editor:—**Is there any contraindication to the use of "pyribenzamine hydrochloride" (tripelennamine hydrochloride) or "benadryl hydrochloride" (diphenhydramine hydrochloride) during pregnancy? I have a patient who is severely affected during the ragweed season. During her pregnancy last summer she took both "benadryl" and "pyribenzamine" regularly. In the seventeenth week of her pregnancy she aborted, passing the placenta but no grossly recognizable fetus. Her uterus at the time was enlarged only to half its expected size at that period. She is pregnant again and is beginning to have severe vasomotor rhinitis and asthmatic attacks. Can she take either "benadryl" or "pyribenzamine" for the relief of these symptoms without endangering her pregnancy? I would appreciate an early reply, due to the urgency of the case.**

M.D., New York.

ANSWER.—Both of these drugs have been used extensively during the past year and thus far reports do not indicate that they may produce abortion. In a patient who may have drug sensitization, drug sickness may ensue which, it could be assumed, might of itself have some undesirable effect in pregnancy. This is true of any illness during the antepartum period. In the present instance it is probable that the patient is not in this category, since it was administered during the previous pregnancy.

POSSIBLE CONGENITAL DIVERTICULUM OF THE BLADDER

To the Editor:—**I have under my care a boy 3½ years of age, who passed bloody urine on one occasion about two years ago, but since has had no further urinary symptoms. A presumably congenital diverticulum of the bladder was demonstrated by urogram. He now complains occasionally of mild pain below the navel. Since no other explanation can be found, it is thought that the pain might be caused by the diverticulum. Do you feel that, in the absence of symptoms, surgery is advisable? At what age should this surgery be undertaken, if at all?**

M.D., California.

ANSWER.—One may not presume that a diverticulum of the bladder is congenital. Cystoscopic observation is imperative in the given case. An obstructive lesion at the bladder neck may have caused the diverticulum and may now be causing irreparable pathologic change of the upper part of the urinary tract in addition to the pain below the navel. Among the obstructive lesions in a child aged 3½ years one may mention: contracture of the vesical neck; bands, folds or valves of the posterior urethra; hypertrophy of the verumontanum; meatal stricture; preputial stricture, and anterior urethral stricture.

To complete the examination retrograde pyelograms should be made and differential renal function should be ascertained to establish the integrity of the upper part of the urinary tract.

If an obstructing lesion is found it should be corrected regardless of age. Subsequently, the diverticulum may not need surgical correction.

THE SEDIMENTATION RATE DURING PREGNANCY

To the Editor:—**Is blood drawn from the vein as accurate for use in taking a blood count as the usual prick of the finger? How much does the normal sedimentation rate rise during pregnancy, and when must pregnancy be taken into consideration when evaluating the moderately rapid sedimentation rate due to other causes such as rheumatic fever?**

M.D., New Jersey.

ANSWER.—Blood drawn from the vein and introduced into a proper anticoagulant is an accurate and reliable source for the determination of the red count, white count, hematocrit, platelet count and certain other observations. It is more reliable than samples obtained by capillary puncture. The anticoagulant of choice is dry oxalate mixture, which is made as follows: Three grams of crystalline ammonium oxalate and 2 Gm. of crystalline potassium oxalate are dissolved in distilled water with the aid of heat and made to a final volume of 100 cc. This gives a final concentration of 5 Gm. per hundred cubic centimeters of mixed oxalates. The concentration used in blood is 200 mg. of oxalate mixture per hundred cubic centimeters of whole blood. The standard amount of blood taken for hematologic observations is 5 cc. For convenience, the following procedure is used: A stock of bottles or tubes is prepared in advance to receive 5 cc. samples of blood by pipetting into each receptacle 0.2 cc. of the solution of oxalate mixture and drying the anticoagulant in the room, in a desiccator or in an oven, using a temperature of less than 180 C. When dry, stoppers are added. Receptacles containing dry oxalate mixture can be stored indefinitely without deterioration.

WARNING: Dry oxalate mixture cannot be used for any chemical test in which nitrogen determinations are made, since it contains ammonia.

The sedimentation rate of red blood cells increases during the last trimester of pregnancy in a gradual and progressive manner, reaching a maximum immediately after delivery. It then decreases to normal, but this may require a period of several weeks. This is related to an increase in the concentration of plasma fibrinogen during the latter portion of pregnancy and the puerperium. Therefore, a moderate elevation of sedimentation rate occurring during the last half of pregnancy must be considered as possibly related to the pregnancy itself. For both the question concerning the anticoagulant and that concerning the sedimentation rate, reference is made to Wintrobe, M. M.: Clinical Hematology, edition 2, Philadelphia, Lea & Febiger, 1946.

DAMAGE TO SIGHT AND HEARING FROM ELECTRIC SHOCK

To the Editor:—**A man aged 23 came in with unilateral deafness and poor vision (20/200) in the eye on the same side as the deafness. His history was "being struck by a wire carrying 275 volts direct current over that ear alongside the head." Two men had been killed previously by the same type of accident. Examination revealed total deafness in the left ear but no perforation of the tympanic membrane. Eye examination revealed no fundus lesion and vision could not be improved. The patient's past history was that he has been discharged from the navy with normal vision. This accident put him in the hospital for nine days. Could an electric shock such as this cause an injury to produce deafness and blindness?** **M.D., West Virginia.**

ANSWER.—An electric shock of 275 volts, with sufficient amperage, could cause such a condition. The fact that two men had been killed by such a shock is evidence that the amperage was high. Damage is often on both sides with diffusion of the electric shock, but a local shock, leaving no severe skin burn, can cause severe damage to deeper structures. If the caloric labyrinth tests produce no nystagmus there is presumptive evidence of eighth nerve damage. Severe optic nerve damage can occur from electric shock. Such cases later show the picture of optic atrophy.

SUBACUTE NEPHRITIS

To the Editor:—**A man, 29, in good general physical condition, has had subacute nephritis for the last six months. The onset presumably followed a streptococcic tonsillitis. Some improvement followed the usual dietary measures and a course of penicillin, 150,000 units, over a period of seven days. He still has albumin (3 plus), with red and white blood cells and some renal epithelia in his urine. His blood pressure has varied within fairly normal limits, and there has been transient moderate increase in nitrogen urea, uric acid and creatinin. Eye grounds have been essentially normal. The tonsillar stumps are buried and there is moderate adenopathy in cervical lymph nodes. Although several cultures have been made from specimens of catheterized urine on only one occasion has a streptococcus been recovered. The question of complete surgical removal of the tonsillar stumps arises, and I would appreciate an opinion as to its advisability. Would the risk of causing the renal disease to flare up be diminished by a preoperative course of penicillin?** **Rudolph V. Gorsch, M.D., New York.**

ANSWER.—The advisability of immediate complete removal of the infected tonsillar stumps cannot be dogmatically affirmed or denied. Certainly it would be desirable to remove these foci of infection which may be constantly reinfecting the kidneys, but there is hazard in the probability of a bacteremia induced by trauma to the infected throat. It would appear more desirable to attempt first more intense antibiotic therapy with penicillin, 40,000 units every three hours for five or six days. After this, urinary, throat and blood cultures as well as estimation of the renal functional capacity should be carried out. If tonsillectomy is to be performed at a later date, both preoperative and postoperative administration of penicillin is desirable.

Unfortunately, no mention is made of any examination of the blood, either by culture or routine hematologic methods. Anemia is an almost universal consequence of acute nephritis, and its continuance plays an important role in the perpetuation of the disorder. Injured structures can hardly be expected to repair themselves effectively unless they are obtaining a nearly optimum blood supply. If anemia coexists, as it most probably does, it should be energetically combated, even to the administration of whole blood by transfusion.

IN VIVO AND IN VITRO STREPTOMYCIN RESISTANCE OF TUBERCLE BACILLI

To the Editor:—In many institutions where streptomycin is used for tuberculosis the value of continued treatment is judged by culture resistance of the involved organism. Has any work been done which indicated that resistance in vivo is definitely a corollary of any resistance which may be found in vitro? Lester Leonard, M.D., Miami Beach, Fla.

ANSWER.—The exact relation between the in vivo and in vitro resistance of tubercle bacilli to streptomycin in man is not apparent as yet. However, the resistance developed to streptomycin by tubercle bacilli from 8 of 12 patients ranged from five hundred to a thousand times as great as that of cultures taken before treatment (Youmans and associates). This resistance is retained even after residence in guinea pigs for ten weeks or more and may subsequently be maintained on glycerinated egg yolk agar for many weeks (Karlson, Feldman and Hinshaw). Even in vitro there is a wide variation in the rate of resistance development, ranging from twofold to a thousandfold (Williston and Youmans). It was noted recently that "the clinical significance of the resistance to streptomycin developed by tubercle bacilli is not definitely established" (Youmans and Karlson) after a study of 131 strains prior to treatment (90 per cent being inhibited in concentrations of less than 2 micrograms per cubic centimeter medium); a small number of strains were isolated and tested following treatment with streptomycin, some attaining a resistance of about 2,000 micrograms. In white mice streptomycin-resistant human tubercle bacilli were found to be as virulent as streptomycin-sensitive strains, and infection with these streptomycin-resistant cultures was not suppressed by treatment of the mice with streptomycin (Youmans and Williston).

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SMALL FEMALE BREASTS

To the Editor:—A woman, aged 22, who has been previously married and has a child 3 years of age, complains of very small breasts. Physical examination presents no abnormalities other than the one of which she complains. The mammary glands are hardly larger than those of a male. The patient is so concerned about this condition that it is becoming an obsession with her and she is developing a neurotic condition. I have hesitated to use hormonal treatment because it was felt that no definite results could be promised. Will you please outline any possible hormonal treatment that may be of value in this case.

M.D., Alabama.

ANSWER.—It can be stated rather definitely that hormonal therapy, that is, estrogens, will induce growth of the breast only in those patients who have an estrogen deficiency—for example, those with infantile sexual organs or those in the climacteric. The administration of estrogens to a normally menstruating woman seldom gives rise to growth of the breast, although it is possible that massive doses may induce some engorgement of the breast similar to that seen in chronic cystic mastitis. Nevertheless, in those patients in whom the breasts respond to the administration of estrogens there is a recession in size following the cessation of therapy.

TREATMENT OF MERCURY POISONING

To the Editor:—A child 3 years of age ate 2 teaspoonfuls of ointment of ammoniated mercury. What is the treatment? M.D., Massachusetts.

ANSWER.—Two teaspoonfuls of either the 5 or 10 per cent ammoniated mercury ointment contains sufficient mercury to prove fatal to an adult. Ammoniated mercury is about equal in toxicity to bichloride of mercury and in fact, due to the method of manufacture, may contain appreciable quantities of the latter. As variously formulated, this ointment may have as its base only petrolatum, an indigestible but emulsifiable fat, or instead, petrolatum along with hydrous wool fat, a digestible fat. In either case an undetermined portion of the mercury may leave the alvine tract unabsorbed. Notwithstanding, prompt emesis and repeated gastric lavage are indicated. Promptly also BAL (2,3-dimercaptopropanol) injections should be given. The dose most recommended is 1.2 cc. of the 10 per cent solution per 100 pounds (45.4 Kg.) of weight, introduced intramuscularly four times daily for two days and diminished thereafter. Thus the dose for a 30 pound (13.6 Kg.) child would approximate 0.4 cc. Best results are to be expected if treatment is begun within three or four hours. Delayed treatment with BAL still may be of some value. The total experience in the BAL therapy of mercury poisoning, particularly in children, is so limited that categoric statements may not be made. Any further treatment should be on a symptomatic basis.

STREPTOMYCIN AND RENAL TUBERCULOSIS

To the Editor:—Kindly advise me about the use of streptomycin in renal tuberculosis. What dosage is advisable and how long should treatment last? A. A. Skemp, M.D., LaCrosse, Wis.

ANSWER.—Streptomycin has been used to a limited extent in the treatment of renal tuberculosis. In the report of Feldman (*J. Roy. Inst. Pub. Health & Hygiene* **9**:267, 297 and 343, 1946) from data supplied by Hinshaw up to May 1946, 14 patients had been treated with apparently favorable response in 8. The improvement consisted in a decrease in pyuria and in the number of bacilli excreted; in cases in which the bladder was involved the urinary frequency was decreased and the capacity of the bladder increased. In 6 of the improved patients the process was not arrested, whereas in 2 it was possibly arrested. The dosage of streptomycin for treatment in these cases is 1.5 to 2 Gm. a day for eight to twelve weeks.

TREATMENT OF CONDYLOMATA ACUMINATA WITH PODOPHYLLIN

To the Editor:—In some recent publication, which I have misplaced, there was an article relative to condyloma acuminatum and its treatment with podophyllin suspended in liquid paraffin. Please comment on the effectiveness of this treatment and inform me of the proportion and preparation of the proposed treatment.

C. P. McKenzie, M.D., Mexia, Texas.

ANSWER.—In a paper entitled "A Study of the Effects of Podophyllin on Normal Skin, Condylomata Acuminata and Verrucae Vulgaris" (*Arch. Dermat. & Syph.* **56**:30 [July] 1947), Sullivan and King described the various methods of treatment with podophyllin. There is also discussion of modifications of treatment by various dermatologists at the end of this article. The use of podophyllin was probably first introduced by Kaplan in 1942 (Culp, O. S. and Kaplan, I. W.: Condylomata Acuminata. Two Hundred Cases Treated with Podophyllin. *Ann. Surg.* **120**:251 [Aug.] 1944). In regard to the cytologic effects of podophyllin (Sullivan, B. J. and Wechsler, H. L.: The Cytological Effects of Podophyllin. *Science* **106**:433 [April 25] 1947), reports by numerous authors on the use of this drug in various vehicles in the treatment of condyloma acuminatum have, on the whole, been most favorable. Careful attention must be given to the various technics of application in order to avoid untoward results.

TESTOSTERONE IN TREATMENT OF SCHIZOPHRENIA

To the Editor:—Has testosterone proprionate been used in the treatment of schizophrenia? If so, I would like a bibliography.

Bryce P. Weldy, M.D., Hartford City, Ind.

ANSWER.—Testosterone propionate has been tried in the treatment of schizophrenia but not extensively. There has not been much indication to use it except in those cases in which there was hypogonadism. A single report by Sutherland and Hoskins was good, but the follow-up has been only for two months. Guirdham reported 4 cases, in 2 of which patients with schizoid elements showed pronounced improvement after treatment with testosterone; on another occasion he reported 3 cases, 1 that of a catatonic schizophrenic person, who responded well. It is probable that the cases in which such treatment is indicated are exceedingly few. The bibliography is as follows:

Guirdham, A.: Function of Testosterone in Mental Disease. Bristol Med. Chir. J. no. 220, **59**: 1-6, 1942.

Guirdham, A.: Treatment of Mental Disorders with Male Sex Hormones. Brit. M. J. **1**: 10-12 (Jan. 6) 1940.

Helman, S.: Dementia Praecox with Hypogonadism Treated with Testosterone Propionate. South African M. J. **13**: 745 (Nov. 11) 1939.

Randall, L. O.: Effect of Testosterone on Serum Lipids in Schizophrenia, **133**: 137-140 (March) 1940.

Sutherland, G. F., and Hoskins, R. G.: A Case of Schizophrenia in a Hypogonad Man, J. Clin. Endocrinol. **2**: 647-648 (Nov.) 1942.